

PATENT COOPERATION TREATY
PCT
INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference YCT-469	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP00/00510	International filing date (day/month/year) 31/01/2000	Priority date (day/month/year) 29/01/1999	
International Patent Classification (IPC) or national classification and IPC C08F20/36			
Applicant AMERSHAM PHARMACIA BIOTECH K.K. et al.			
1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of 9 sheets, including this cover sheet. <input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of 54 sheets.			
3. This report contains indications relating to the following items: I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input checked="" type="checkbox"/> Lack of unity of invention V <input type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input checked="" type="checkbox"/> Certain documents cited VII <input checked="" type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application			

Date of submission of the demand 10/07/2000	Date of completion of this report 12.04.2001
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PATENT COOPERATION TREATY

PK9931

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing (day/month/year)	12.04.2001
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Applicant's or agent's file reference
YCT-469

IMPORTANT NOTIFICATION

International application No.
PCT/JP00/00510

International filing date (day/month/year)
31/01/2000

Priority date (day/month/year)
29/01/1999

Applicant
AMERSHAM PHARMACIA BIOTECH K.K. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP00/00510

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-7,10-12,14-28, as originally filed
30-37,39-55,
57-98

9,13,38,56	as received on	06/02/2001	with letter of	06/02/2001
8,29	as received on	13/02/2001	with letter of	09/02/2001

Claims, pages:

105-110,132,135, as originally filed
137,139-151,
154-156

103,119,125	as received on	06/02/2001	with letter of	06/02/2001
99,100,100a,101, 101a,102,102a,104, 111,111a,112,112a, 113-118,118a,120, 120a,121,122,122a, 123,124,124a,126, 127,127a,128,129, 129a,130,130a,131, 133,133a,134,136, 136a,138,152,153, 153a	as received on	13/02/2001	with letter of	09/02/2001

Drawings, sheets:

1/15-15/15 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
 the language of publication of the international application (under Rule 48.3(b)).

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- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c));

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application.
- claims Nos. .

because:

- the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

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see separate sheet

- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - no international search report has been established for the said claims Nos. .
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- the written form has not been furnished or does not comply with the standard.
 - the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:
 - restricted the claims.
 - paid additional fees.
 - paid additional fees under protest.
 - neither restricted nor paid additional fees.
2. This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
 - complied with.
 - not complied with for the following reasons:
see separate sheet
4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:
 - all parts.
 - the parts relating to claims Nos. see Item III..

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

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2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

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Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

A lack of clarity and conciseness of the claims as a whole arises, since the plurality of independent claims (35!) makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection. This objection is also of particular relevance having regard to the multiplicity of embodiments covered by claim 1 which includes **about 30** subgroups of different polymers (see Item IV.).

This deficiency could have been remedied by filing an amended set of claims defining the relevant subject-matter in terms of a minimum number of independent claims in each category followed by dependent claims covering features which are merely optional (Rule 6.4 PCT). However, the applicants choose not to do so.

Re Item IV

Lack of unity of invention

There is a lack of unity of the invention a posteriori.

The single inventive concept of this application may be represented by the fact that the polymers are "temperature-responsive" (whatever this obscure term may mean) due to certain functional groups being attached to the polymer backbone.

Most of the groups of polymers A through E-5 defined in independent claim 1 are already known from the "X" citations of the S.R.. In particular reference is made to:

D1 (US-A-2 458 420; see eg col. 1 and col. 3 line 11),

D3 (EP-A-0 697 400; see eg page 5 lines 40-55),

D6 (US-A-3 721 565; see eg col. 13 lines 6-8, and comonomers No. 136-139, 140 on col. 17, and claim 1),

D7 (US-A-4 062 831; see eg col. 2 lines 15-68, Examples 3 and 12), and

D13 (GB-A-1 409 967; see eg claim 1 wherein R² may acyl or carboxyalkyl)

which all disclose polymers having either ester and/or amido and/or ether groups attached to the polymer backbone.

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The requisite unity of invention (Rule 13.1 PCT) therefore no longer exists inasmuch as a technical relationship involving one or more of the same or corresponding special technical features in the sense of Rule 13.2 PCT does not exist between the groups of polymers specified in claim 1.

The separate inventions thus are:

- 1) Polymers A having an amido group attached to the polymer backbone via an ester group,
- 2) Polymers A having an ester group attached to the polymer backbone via an amido group,
- 3) Polymers A having attached to the polymer backbone diester groups,
- 4) Polymers B having attached to the polymer backbone diamido groups,
- 5) Polymers C-1 having attached to the polymer backbone amido group(s) and being crosslinked via one amido group,
- 6) Polymers C-1 having attached to the polymer backbone ester group(s) and being crosslinked via one ester group,
- 7) Polymers C-1 having attached to the polymer backbone ether group(s) and being crosslinked via one ether group,
- 8) Polymers C-1 having attached to the polymer backbone amido and ester groups and being crosslinked via one amido group,
- 9) Polymers C-1 having attached to the polymer backbone amido and ester groups and being crosslinked via one ester group,
- 10) Polymers C-1 having attached to the polymer backbone amido and ether groups and being crosslinked via one amido group,
- 11) Polymers C-1 having attached to the polymer backbone amido and ether groups and being crosslinked via one ether group,
- 12) Polymers C-1 having attached to the polymer backbone ester and ether groups and being crosslinked via one ester group,
- 13) Polymers C-1 having attached to the polymer backbone ester and ether groups and being crosslinked via one ether group,
- 14) Polymers C-1 having attached to the polymer backbone amido and ester and ether groups and being crosslinked via one amido group,
- 15) Polymers C-1 having attached to the polymer backbone amido and ester and ether groups and being crosslinked via one ester group,

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- 16) Polymers C-1 having attached to the polymer backbone amido and ester and ether groups and being crosslinked via one ether group,
- 17) Polymers C-2 having attached to the polymer backbone a diamido group,
- 18) Polymers C-2 having an amido group attached to the polymer backbone via an ester group,
- 19) Polymers C-2 having an amido group attached to the polymer backbone via an ether group,
- 20) Polymers D having attached to the polymer backbone an amido group,
- 21) Polymers E-1 having attached to the polymer backbone amido groups including a tertiary amido group,
- 22) Polymers E-2 having attached to the polymer backbone amido groups including a tertiary amido group,
- 23) Polymers E-2 having attached to the polymer backbone amido groups and ester groups including a tertiary amido group,
- 24) Polymers E-3 having attached to the polymer backbone amido groups including a tertiary amido group,
- 25) Polymers E-4 having attached to the polymer backbone amido groups including a tertiary amido group,
- 26) Polymers E-4 having attached to the polymer backbone amido groups and ester groups including a tertiary amido group,
- 27) Polymers E-5 having tertiary amido groups attached to the polymer backbone via amido groups,
- 28) Polymers E-5 having tertiary amido groups attached to the polymer backbone via ester groups, and
- 29) Polymers E-5 having tertiary amido groups attached to the polymer backbone via amido and ester groups.

The applicants did not comment upon this objection nor amended the claims in this respect.

Re Item VI

Certain documents cited

EP-A-0 970 945 and WO 00/07002: These documents may become relevant for novelty considerations when entering the regional phase.

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Re Item VII

Certain defects in the international application

It is noted that the applicants did not confirm that all disclaimers ("provisos") introduced into the amended set of claims have been drafted correctly and in close relation to the language and disclosure of the corresponding documents ie it was not confirmed that the disclaimers would not add new subject-matter as required by Art. 19 (2) PCT.

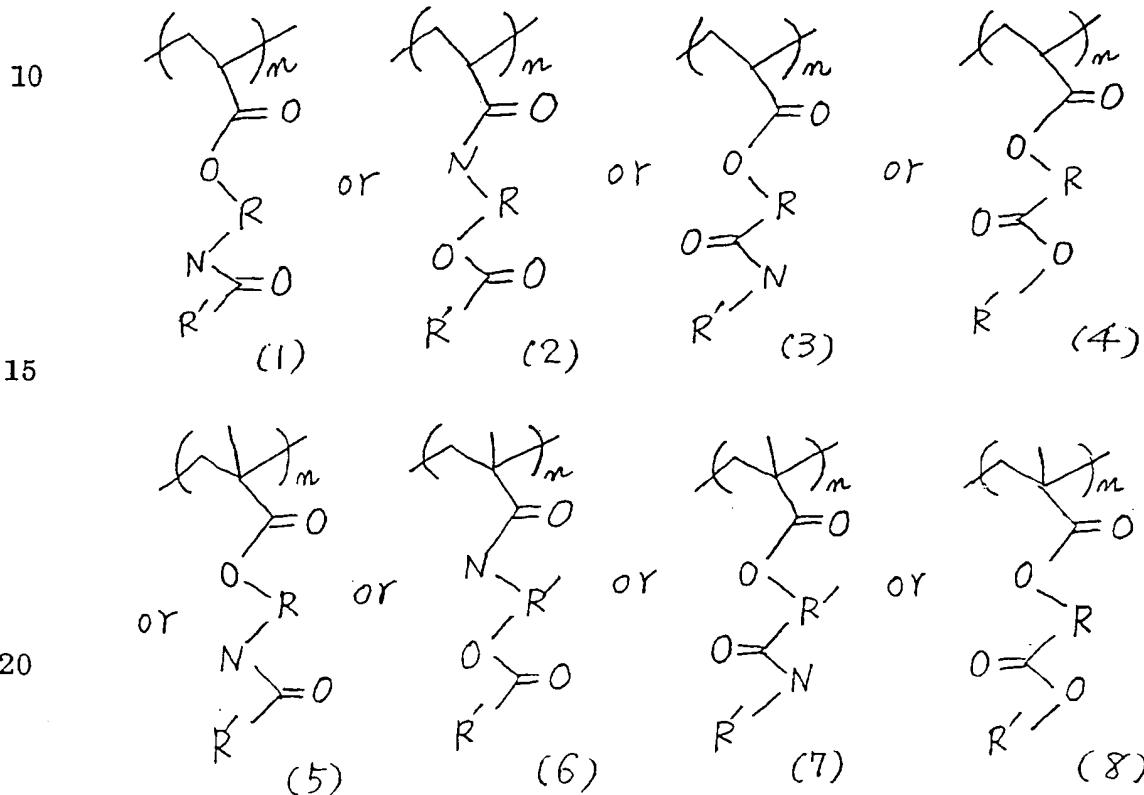
Further, there are the following deficiencies:

1. Line 28 of page 99 of original claim 1 is missing in new claim 1.
2. The reason for introducing into claims 1, 2, 9, 12, 13, and 16 the proviso "R is not derived from the structure of an amino acid" is not evident and has not been explained.
3. Part of line 18 of page 120 (see original claim 16) is missing in new claim 16.
4. The structures of group B has not been corrected in claim 30 (cf. page 128).
5. Part of line 26 of page 129 (se original claim 33) is missing in new claim 33.
6. The first line of original claim 48 is missing on new page 138.

the separation of various substances. The present invention has been completed based on these findings.

Accordingly, the present invention provides a polymer compound comprising polymer subunits as defined in groups A-E and with the total or relative number of individual monomer units as given.

Group A:



wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic

hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, 5 one or more hydroxyl groups and 3 to 9 carbon atoms; and n is an integer of 2 or above.

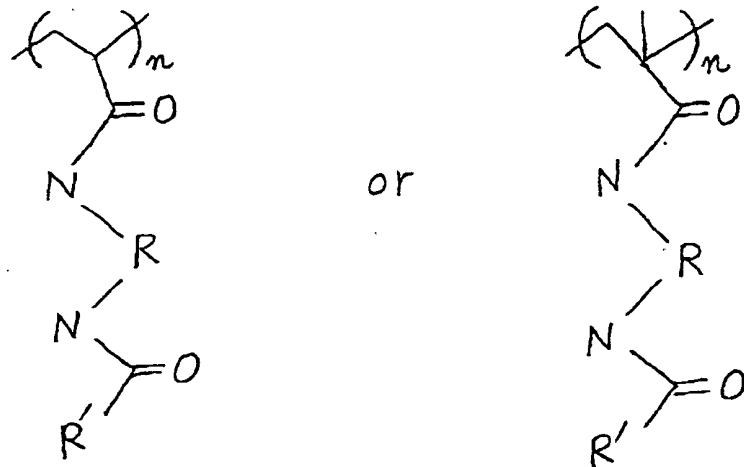
Group B:

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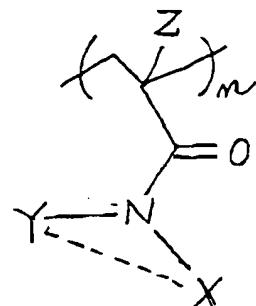
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wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group

Group D:

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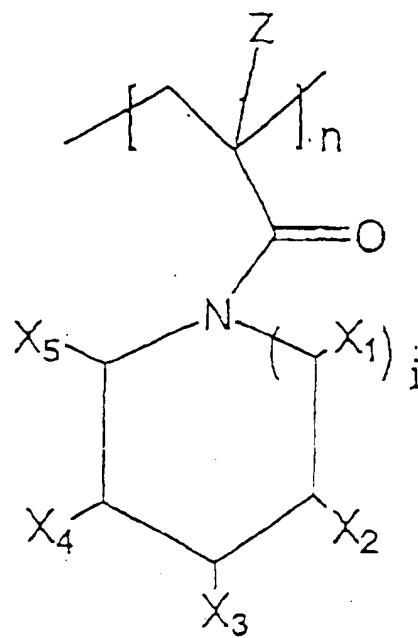


wherein Z represents a hydrogen atom or a methyl group; X
 10 represents a hydrogen atom or a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms and carrying at least one hydroxyl group; Y represents a linear or branched aliphatic hydrocarbon group having 2 to 8 carbon atoms and carrying at least one hydroxyl group, or X and Y may form together
 15 a chemical bond; and n is an integer of 2 or more.

Group E-1:

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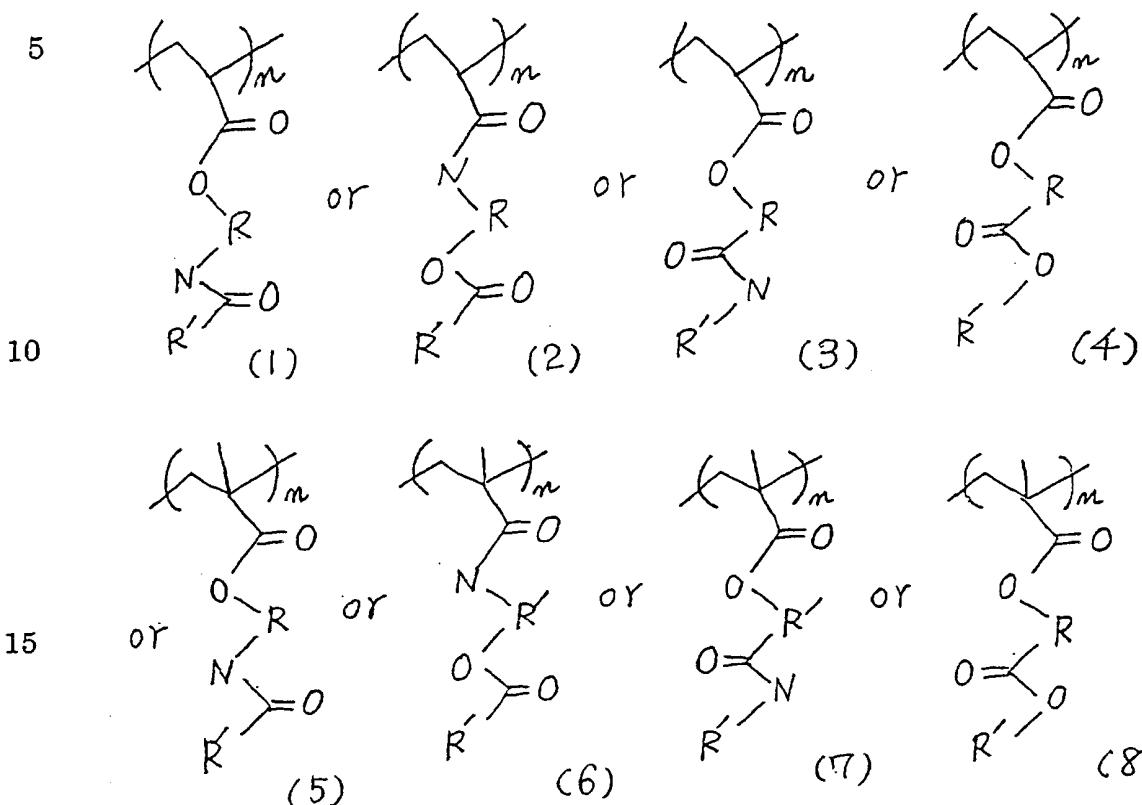
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has the following structure.

1. Compounds represented by the formula of Group A.

Group A:

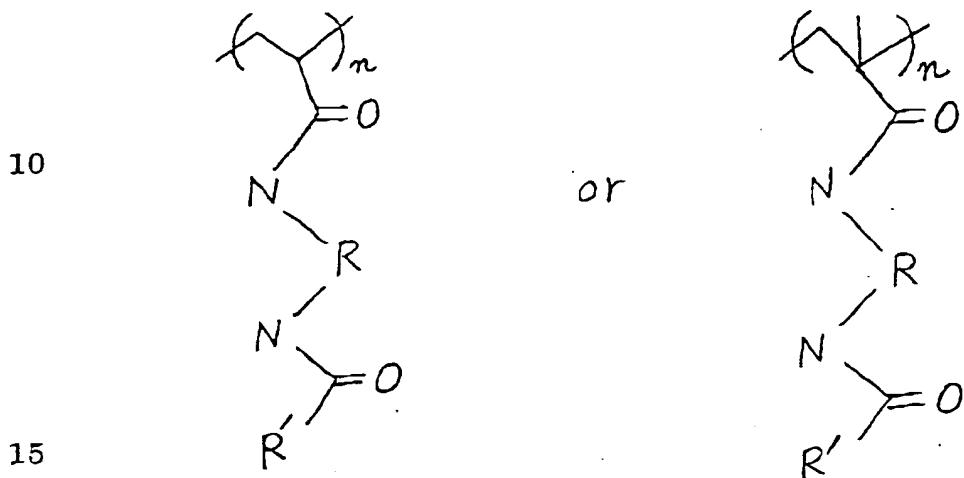


wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon

formation of the hydration water in the side chain or the intramolecular or intermolecular interaction among the polymer chains.

5 2. Compounds represented by the formula of Group B.

Group B:



wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a 20 divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group 25 having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, one or more hydroxyl groups and 3 to 9 carbon atoms; and n is

possible in this step to dissolve a chain transfer agent in the polymerization solvent so as to control the molecular weight of the polymer compound or to introduce a reactive functional group to the terminal of the polymer compound. Materials containing 5 the thus obtained polymer compounds are applicable to adsorption and separation materials such as various liquid chromatographic packings, drug carriers, dielectric and magnetic materials, piezoelectric and pyroelectric materials, degradable and reactive materials, biofunctional materials, etc.

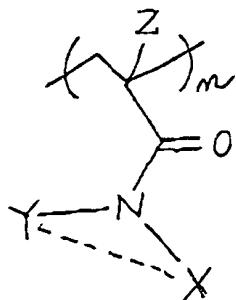
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4. Compounds represented by the formula of Group D.

The polymer compound according to the present invention has the following structure. Namely, a polymer material comprising a polymer compound consisting exclusively of a 15 repeating unit represented by the following formula (I) or a copolymer or a gel containing this unit structure and showing temperature-responsiveness in a solution.

Group D:

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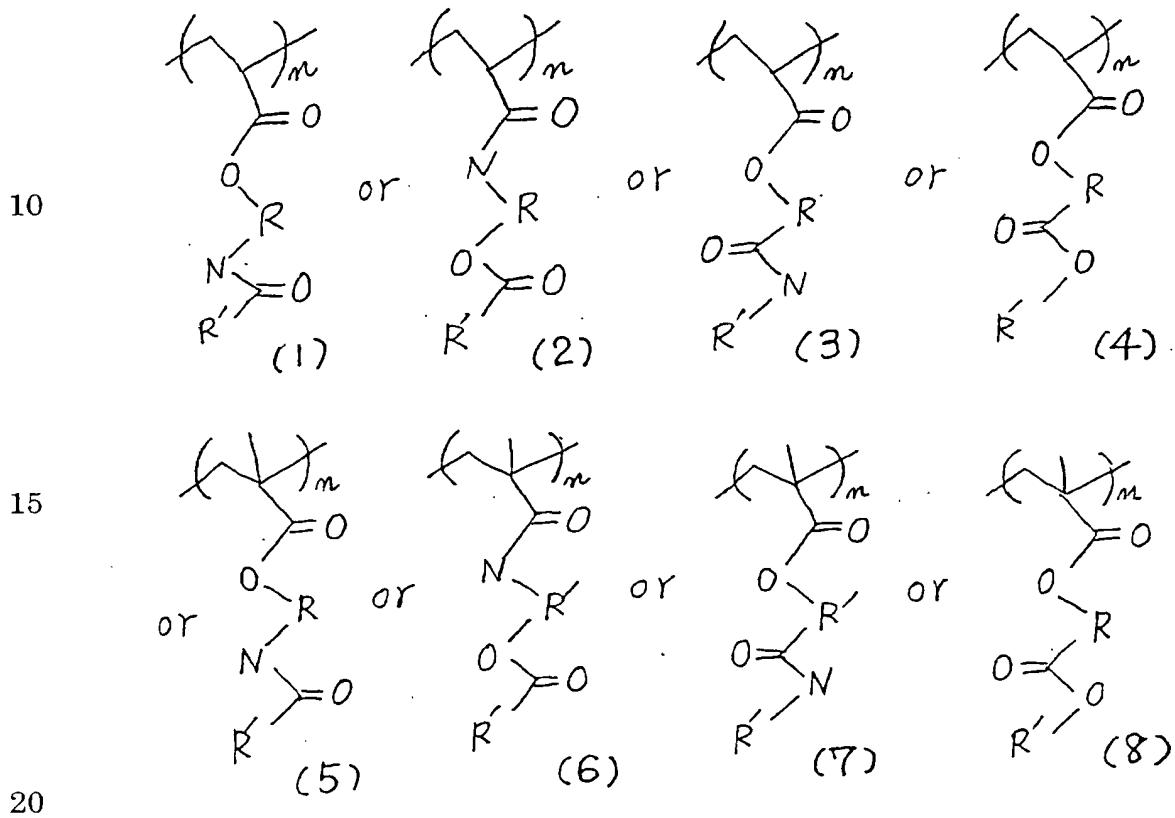
wherein Z represents a hydrogen atom or a methyl group; X represents a hydrogen atom or a linear or branched aliphatic

CLAIMS

1. (amended) A polymer compound selected from the following groups:

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Group A:



wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms;

25 R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group

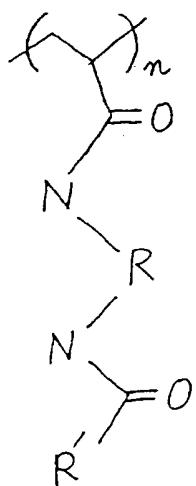
9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, one or more hydroxyl groups and 3 to 9 carbon atoms; and n is an integer of 2 or above; provided that R is not derived from
 5 the structure of an amino acid, provided that when the R' of formula (1) or (5) of Group A represents a linear or branched aliphatic carbon group having 1 to 8 carbon atoms and n is an integer of 2-4, the aliphatic carbon group does not carry any hydroxyl group, provided that when the R of formula (3) or (7)
 10 represents an ethylene group (-CH₂CH₂-), R' represents a linear or branched aliphatic carbon group having 1 to 8 carbon atoms which group carries at least one hydroxyl group, and provided that the compounds of formula (3) or (7) wherein R represents a branched ethylene group (-CH(CH₃)-) are excluded.

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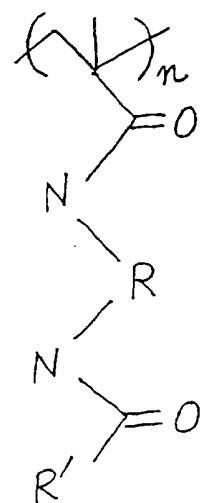
Group B:

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or

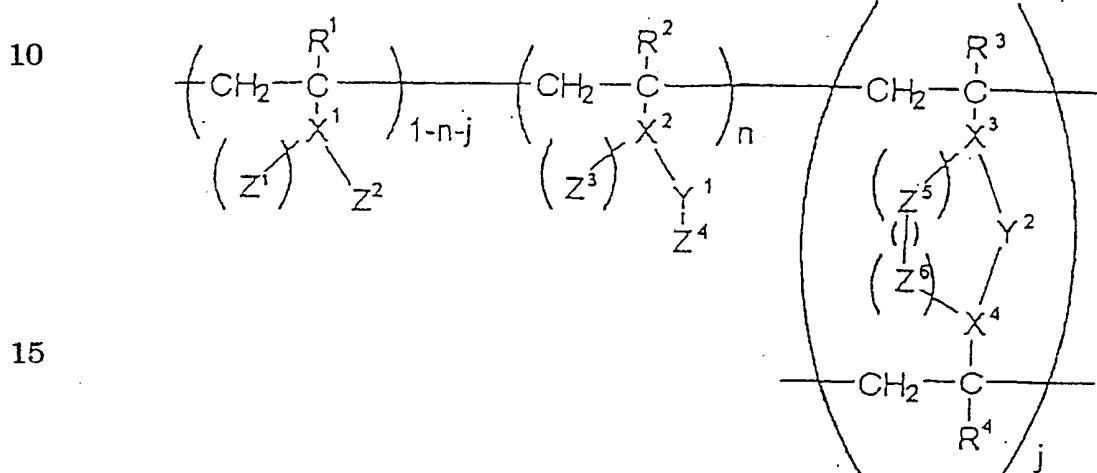


wherein R represents a linear or branched divalent aliphatic

hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group
5 having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon
10 group having one or more acid amide bonds and/or ester bonds,

one or more hydroxyl groups and 3 to 9 carbon atoms; and n is an integer of 2 or above; provided that R is not derived from the structure of an amino acid, and provided that when R represents an methylene group (-CH₂-), R' represents a 5 hydroxymethyl group (-CH₂-OH) or a hydroxyethyl group (-CH₂CH₂-OH).

Group C-1:



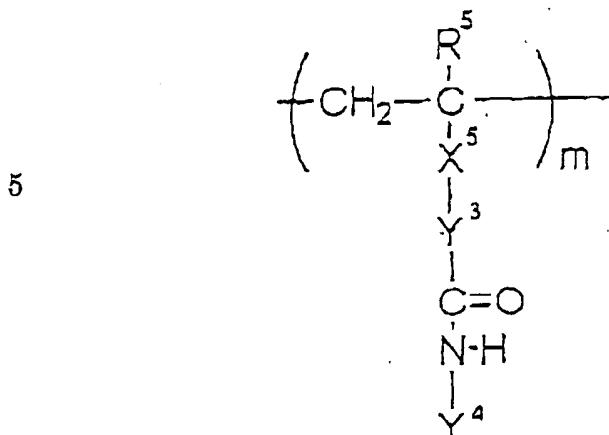
wherein n is the number of the middle kind of monomer unit, j 20 is the number of the right kind of monomer unit, n is from 0.005 to 0.995 (inclusive)and j is from 0 to 0.5 (inclusive); R¹, R², R³ and R⁴ are the same or different and each represents a hydrogen atom or a methyl group; X¹, X², X³ and X⁴ are the same or different and each represents an acid amide group, an ester group or an ether group; Y¹ represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms 25 or a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms.

atoms; Y² represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, a linear or branched divalent aliphatic hydrocarbon group having 1 to 8

carbon atoms and one or more ether groups or a linear or branched
divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms
and one or more hydroxyl groups; Z^1 , Z^2 , Z^3 , Z^5 and Z^6 are the same
or different and each represents a hydrogen atom, a linear or
5 branched aliphatic hydrocarbon group having 1 to 8 carbon atoms,
a linear or branched aliphatic hydrocarbon group having 1 to 8
carbon atoms and one or more hydroxyl groups, a linear or
branched alicyclic hydrocarbon group having 1 to 8 carbon atoms
and one or more hydroxyl group, a linear or branched aliphatic
10 hydrocarbon group having 1 to 8 carbon atoms and one or more ether
groups, a linear or branched alicyclic hydrocarbon group having
1 to 8 carbon atoms and one or more ether groups, a glycoside
having 3 to 12 carbon atoms or a glycoside having 3 to 12 carbon
atoms and carrying a linear or branched aliphatic hydrocarbon
15 atoms and carrying a linear or branched aliphatic hydrocarbon
group having 1 to 8 carbon atoms, provided that Z^1 , Z^3 , Z^5 and
 Z^6 are functional groups bonded respectively to X^1 , X^2 , X^3 and
 X^4 when they are tertiary amide groups and Z^5 may be bonded to
 Z^6 ; and Z^4 represents a hydrogen atom, a hydroxyl group, an amide
20 group, a nitryl group, a linear or branched aliphatic
hydrocarbon group having 1 to 8 carbon atoms, a linear or
branched aliphatic hydrocarbon group having 1 to 8 carbon atoms
and one or more amide groups, a linear or branched aliphatic
hydrocarbon group having 1 to 8 carbon atoms and one or more
25 carbonyl groups, a linear or branched aliphatic hydrocarbon
group having 1 to 8 carbon atoms and one or more nitryl groups,
or a linear or branched aliphatic hydrocarbon group having 1 to
8 carbon atoms and one or more hydroxyl groups; provided that
when X^1 represents an acid amide group, either Z^1 or Z^2 represents

a hydrogen atom or a glycoside having 3 to 12 carbon atoms, provided that neither Z¹ nor Z² represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms or a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more hydroxyl groups, and provided that when Y¹ represents a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms and Z⁴ represents a aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more amide groups, X² represents an acid amide group.

Group C-2:

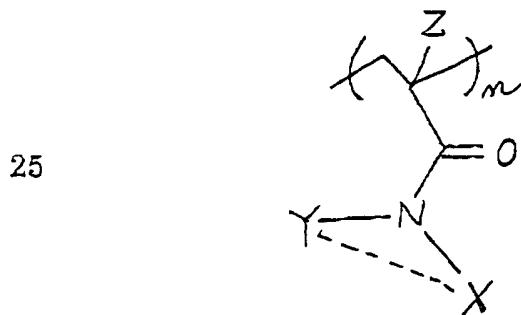


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wherein R⁵ represents a hydrogen atom or a methyl group; X⁵ represents an acid amide group, an ester group or an ether group; Y³ represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms or a divalent 15 alicyclic hydrocarbon group having 3 to 8 carbon atoms; and Y⁴ represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms or a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more hydroxyl groups; n represent an integer 2 or more.

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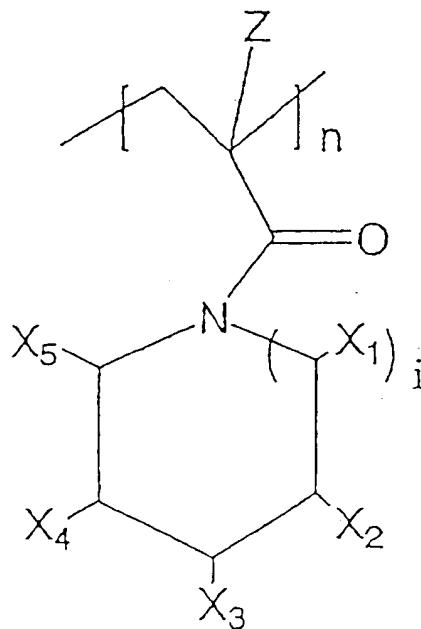
Group D:



wherein Z represents a hydrogen atom or a methyl group; X represents a hydrogen atom or a cyclic hydrocarbon group having 3 to 8 carbon atom and carrying at least one hydroxyl group; Y represents a cyclic hydrocarbon group having 3 to 8 carbon atom and carrying at least one hydroxyl group, or X and Y may form together a chemical bond; and n is an integer of 2 or more.

5 Group E-1:

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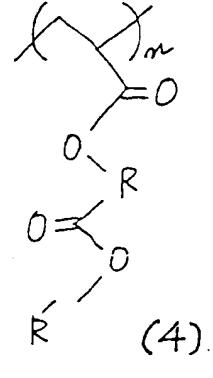
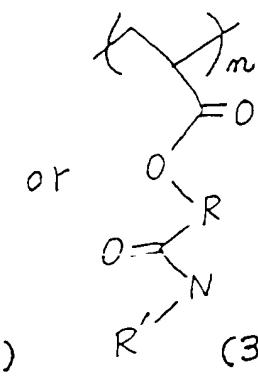
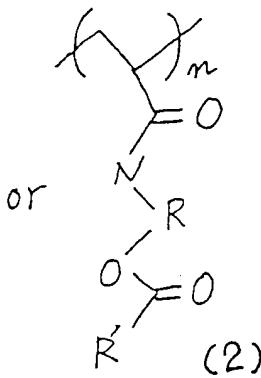
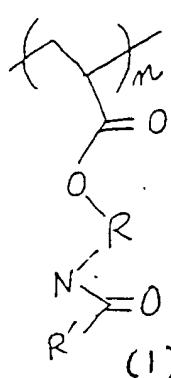
wherein Z represents a methyl group or a hydrogen atom; n is an integer of 2 or more; X₁, X₂, X₃, X₄ and X₅ are the same or different and each represents a hydrogen atom, a group R, or a group - CO-NH-R, provided that at least one of X₁ to X₅ is a group - CO-NH-R (wherein R represents a linear or branched aliphatic hydrocarbon group having 1 to 6 carbon atoms, a linear or

containing at least one amide group, a linear or branched hydrocarbon group having 1 to 8 carbon atoms and containing at least one carbonyl group or a linear or branched hydrocarbon group having 1 to 8 carbon atoms and containing at least one hydroxyl group which may be attached at an arbitrary position,
5 i.e., o-, m- or p-position; provided that when X^1 represents an acid amide group, either Z^1 or Z^2 represents a hydrogen atom or a glycoside having 3 to 12 carbon atoms, provided that neither Z^1 nor Z^2 represents a linear or branched aliphatic hydrocarbon
10 group having 1 to 8 carbon atoms, and provided that when Z^4 represents a aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more amide groups, X^2 represents an acid amide group.

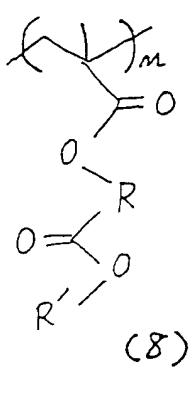
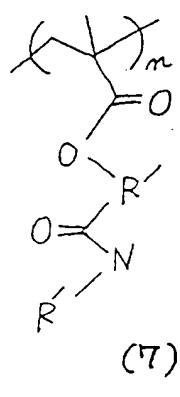
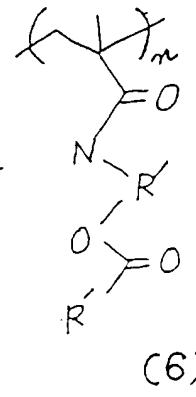
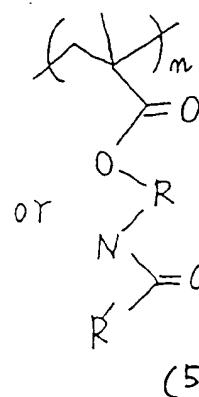
15 2. (amended) The polymer compound as claimed in claim 1
which is represented by the following formula:

Group A:

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wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a

divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 5 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, one or more hydroxyl groups and 3 to 9 carbon atoms; and n is 10 an integer of 2 or above; provided that R is not derived from the structure of an amino acid, provided that when the R' of formula (1) or (5) of Group A represents a linear or branched aliphatic carbon group having 1 to 8 carbon atoms and n is an integer of 2-4, the aliphatic carbon group does not carry any 15 hydroxyl group, provided that when the R of formula (3) or (7) represents an ethylene group (-CH₂CH₂-), R' represents a linear or branched aliphatic carbon group having 1 to 8 carbon atoms which group carries at least one hydroxyl group, and provided that the compounds of formula (3) or (7) wherein R represents 20 a branched ethylene group (-CH(CH₃)-) are excluded.

3. The polymer compound as claimed in Claim 2 which has functional group(s) at the polymer chain terminal.

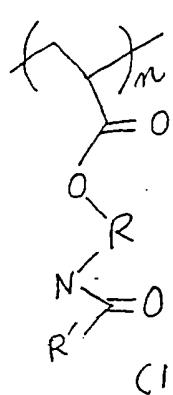
25 4. The polymer compound as claimed in Claim 3, wherein said functional groups are one or more groups selected from the group consisting of carboxyl, amino and hydroxyl groups.

5. The polymer compound as claimed in any of Claims 2 to 4 which has acid amide bonds at two or more sites in the polymer side chain.

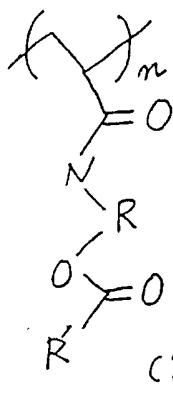
5 6. A heat-responsive polymer material which contains a polymer compound represented by the following formula and shows a cloud point due to a temperature change in an aqueous solution:

Group A:

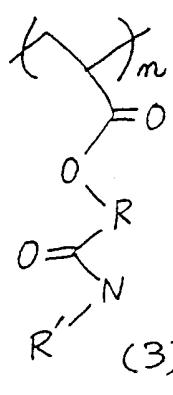
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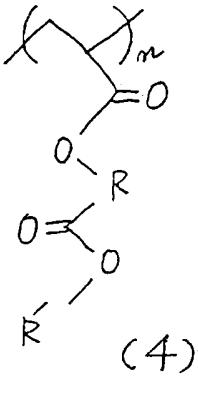
or



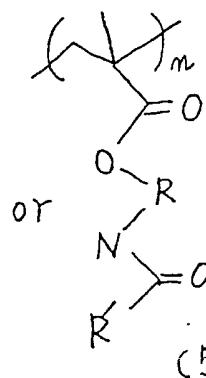
or



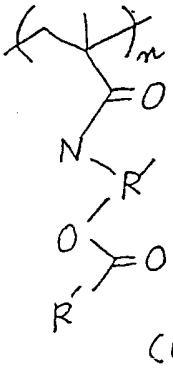
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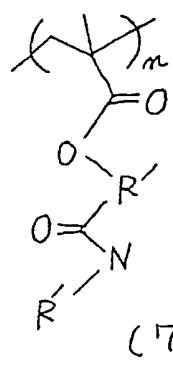
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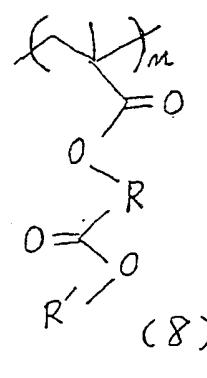
or



or



or



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wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, one or more hydroxyl groups and 3 to 9 carbon atoms; and n is

an integer of 2 or above.

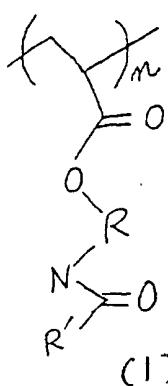
7. The heat-responsive polymer material as claimed in
Claim 6 which has acid amide bond(s) at one or more sites and/or
5 ester bond(s) at one or more sites in the polymer side chain.

8. The heat-responsive polymer material as claimed in
Claim 6 or 7 the polarity of the hydrophilic nature/hydrophobic
nature of which varies at its cloud point and the polarity of
10 which can be controlled depending on the pH value, salt
concentration or the size of R and R'.

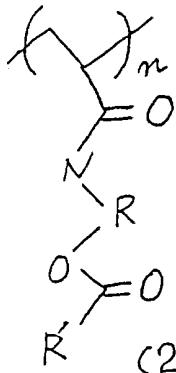
9. (amended) A Chromatographic packing containing a
heat-responsive polymer material which contains a polymer
15 compound represented by the following formula and shows a cloud
point due to a temperature change in an aqueous solution:

Group A:

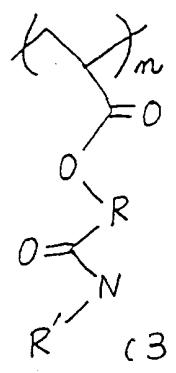
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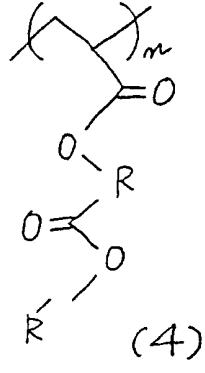
or



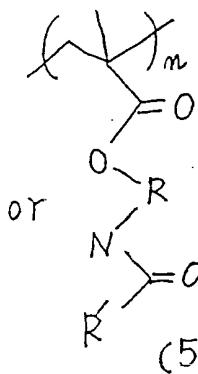
or



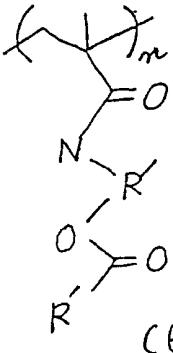
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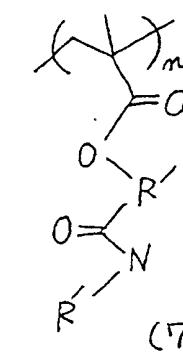
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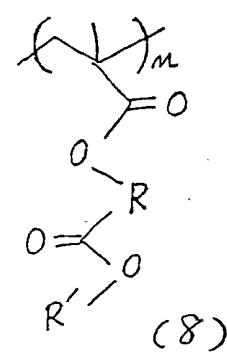
or



or



or



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wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, one or more hydroxyl groups and 3 to 9 carbon atoms; and n is

an integer of 2 or above; provided that R is not derived from the structure of an amino acid, provided that when the R' of formula (1) of Group A represents a linear or branched aliphatic carbon group having 1 to 8 carbon atoms and n is an integer of
5 2-4, the aliphatic carbon group does not carry any hydroxyl group, provided that when the R of formula (3) represents an ethylene group (-CH₂CH₂-), R' represents a linear or branched aliphatic carbon group having 1 to 8 carbon atoms which group carries at least one hydroxyl group, and provided that the compounds of
10 formula (3) wherein R represents a branched ethylene group (-CH(CH₃)-) are excluded.

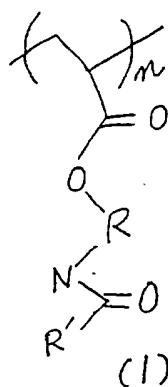
10. A chromatographic packing as claimed in Claim 9 which has acid amide bond(s) and ester bond(s) respectively at one or
15 more sites in the polymer side chain.

11. A method for separating substances characterized by comprising holding a substance on a stationary phase comprising the chromatographic packing as claimed in Claim 8, then changing
20 the hydrophilic/hydrophobic balance of the surface of the stationary phase by the temperature gradient method wherein the external temperature is changed stepwise, and then passing through a single mobile phase, thus effecting separation.

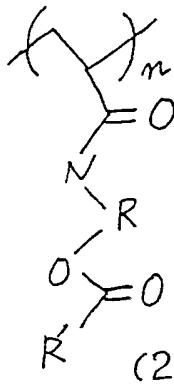
25 12. (amended) A process for producing a polymer compound represented by the following formula:

Group A:

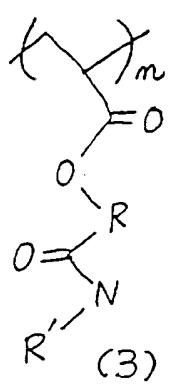
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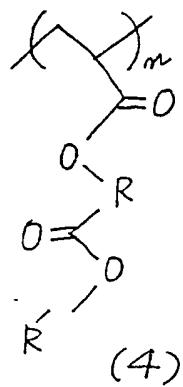
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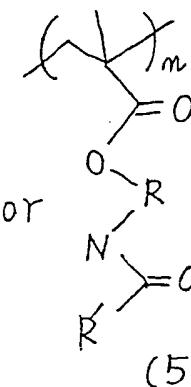
or



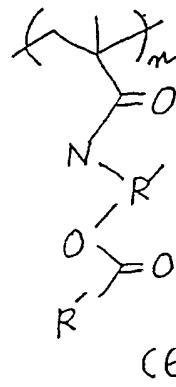
or



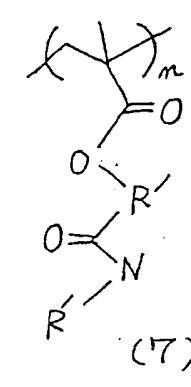
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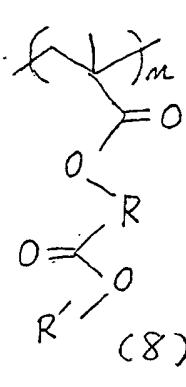
or



or



or



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wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a 20 divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group 25 having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, one or more hydroxyl groups and 3 to 9 carbon atoms; and n is

an integer of 2 or above; provided that R is not derived from the structure of an amino acid, provided that when the R' of formula (1) or (5) of Group A represents a linear or branched aliphatic carbon group having 1 to 8 carbon atoms and n is an 5 integer of 2-4, the aliphatic carbon group does not carry any hydroxyl group, provided that when the R of formula (3) or (7) represents an ethylene group (-CH₂CH₂-), R' represents a linear or branched aliphatic carbon group having 1 to 8 carbon atoms which group carries at least one hydroxyl group, and provided 10 that the compounds of formula (3) or (7) wherein R represents a branched ethylene group (-CH(CH₃)-) are excluded; characterized by using one of the following methods:

(1) reacting a monomer having a primary amino group (for example, 2-aminoethyl methacrylate) with an acid anhydride or 15 lactone and purifying the thus obtained product followed by polymerization in a solvent;

(2) reacting a monomer having a hydroxyl group with an acid chloride and purifying the thus obtained product followed by 20 polymerization in a solvent, said monomer not carrying both a primary acid amide group (-CONH₂) and a hydroxyl group;

(3) reacting an alkylamino alcohol with an acid anhydride, then reacting the thus obtained product with acrylic acid 25 chloride or methacrylic acid chloride and purifying the thus obtained product followed by polymerization in a solvent; provided that step (3) is not applied to the production of the compounds represented by formula (3) or (7) of Group A; or

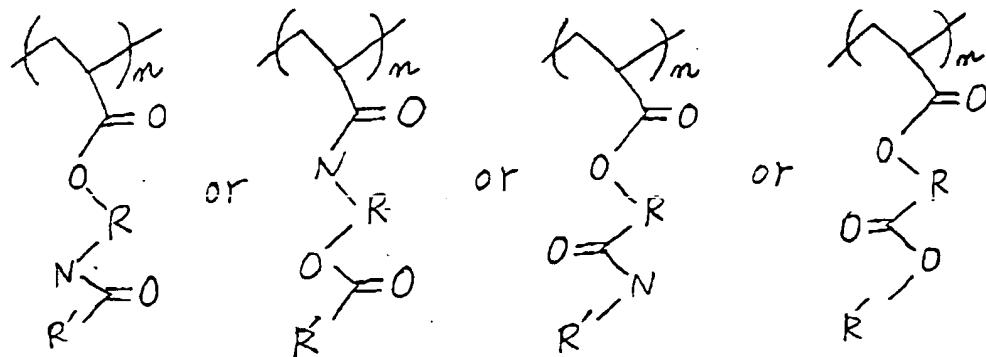
(4) synthesizing a polymer having a primary amino group (for example, poly-2-aminoethyl methacrylate) or its

hydrochloride and reacting the thus synthesized product with an acid anhydride or lactone in a solvent containing triethylamine.

13. (amended) A material for separating or adsorbing
5 biological samples comprising a polymer compound represented by
the following formula and having acid amide bonds at two or more
sites in the polymer side chain:

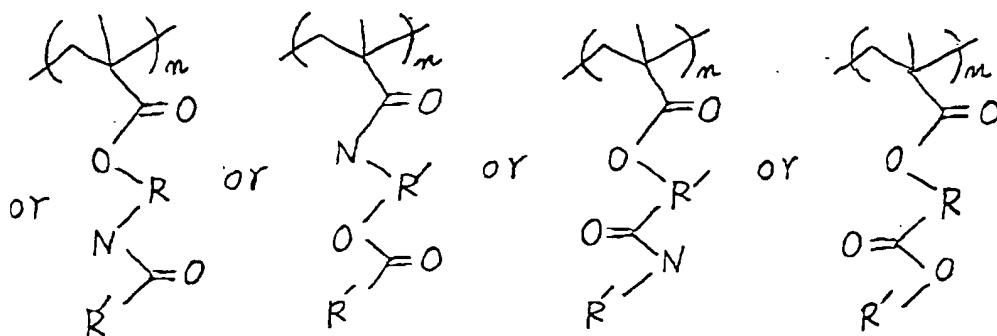
Group A:

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wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a 20 divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds and 2 to 25 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, one or more hydroxyl groups and 3 to 9 carbon atoms; and n is

an integer of 2 or above; provided that R is not derived from the structure of an amino acid, provided that when the R' of formula (1) or (5) of Group A represents a linear or branched aliphatic carbon group having 1 to 8 carbon atoms and n is an
5 integer of 2-4, the aliphatic carbon group does not carry any hydroxyl group, provided that when the R of formula (3) or (7) represents an ethylene group (-CH₂CH₂-), R' represents a linear or branched aliphatic carbon group having 1 to 8 carbon atoms which group carries at least one hydroxyl group, and provided
10 that the compounds of formula (3) or (7) wherein R represents a branched ethylene group (-CH(CH₃)-) are excluded.

14. The material for separating or adsorbing biological samples as claimed in Claim 13 which has functional group(s) at
15 the polymer chain terminal.

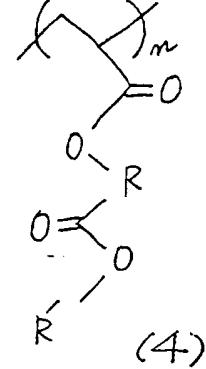
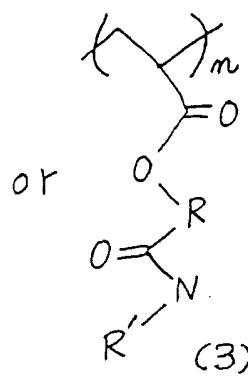
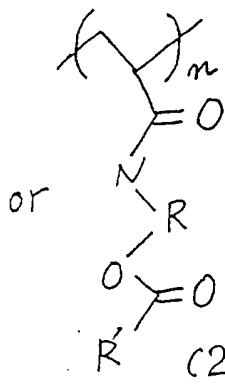
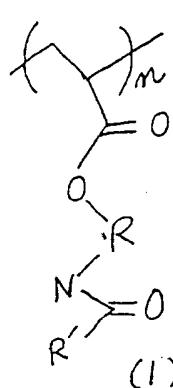
15. The material for separating or adsorbing biological samples as claimed in Claim 14, wherein said functional groups are one or more groups selected from the group consisting of
20 carboxyl, amino and hydroxyl groups.

16. (amended) A method for separating substances characterized by comprising holding a biological sample on a stationary phase, then changing the hydrophilic/hydrophobic balance by changing the external temperature and thus adsorbing and separating the biological sample such as cells, wherein said stationary phase comprises a material for separating or adsorbing biological samples comprising a polymer compound
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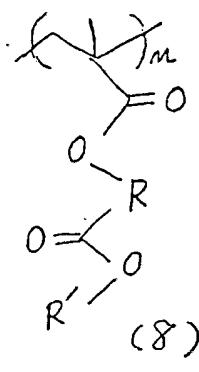
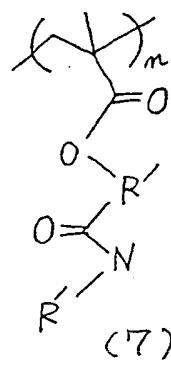
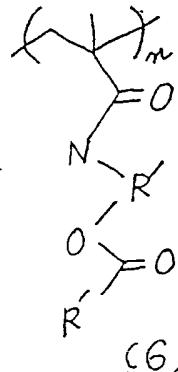
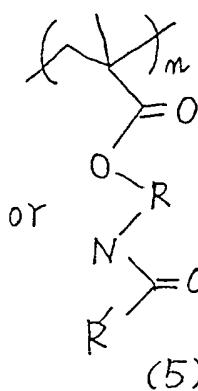
following formula and having acid amide bonds at two or more sites in the polymer side chain:

Group A:

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wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a 20 divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group 25 having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, one or more hydroxyl groups and 3 to 9 carbon atoms; and n is

an integer of 2 or above; provided that R is not derived from the structure of an amino acid, provided that when the R' of formula (1) or (5) of Group A represents a linear or branched aliphatic carbon group having 1 to 8 carbon atoms and n is an
5 integer of 2-4, the aliphatic carbon group does not carry any hydroxyl group, provided that when the R of formula (3) or (7) represents an ethylene group (-CH₂CH₂-), R' represents a linear or branched aliphatic carbon group having 1 to 8 carbon atoms which group carries at least one hydroxyl group, and provided
10 that the compounds of formula (3) or (7) wherein R represents a branched ethylene group (-CH(CH₃)-) are excluded.

17. The method for separating substances as claimed in Claim 16, wherein said polymer compound has functional group(s)
15 at the polymer chain terminal.

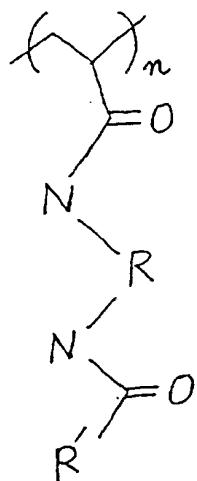
18. The method for separating substances as claimed in Claim 17, wherein said functional groups are one or more groups selected from the group consisting of carboxyl, amino and
20 hydroxyl groups.

19. (amended) The polymer compound as claimed in Claim 1 which is represented by the following formula:

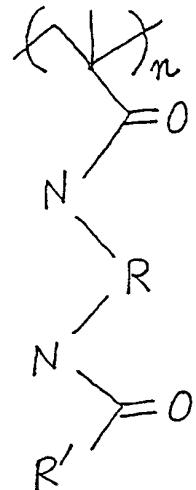
Group B:

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or



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wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms;

R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, one or more hydroxyl groups and 3 to 9 carbon atoms; and n is an integer of 2 or above; provided that when R represents an 10 methylene group (-CH₂-), R' represents a hydroxymethyl group (-CH₂-OH) or a hydroxyethyl group (-CH₂CH₂-OH).

20. The polymer compound as claimed in Claim 19 which has a functional group at the polymer chain terminal.

15

21. The polymer compound as claimed in Claim 20, wherein said functional group is selected from the group consisting of carboxyl, amino and hydroxyl groups.

20

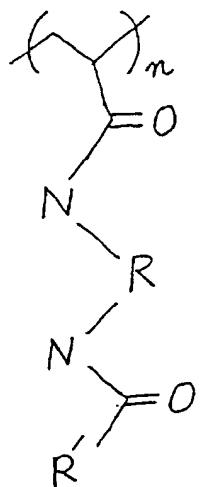
22. The polymer compound as claimed in any of Claims 19 to 21 which has acid amide bonds at two or more sites in the polymer side chain.

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23. (amended) A heat-responsive polymer material which contains a polymer compound represented by the following formula and shows a cloud point due to a temperature change in an aqueous solution:

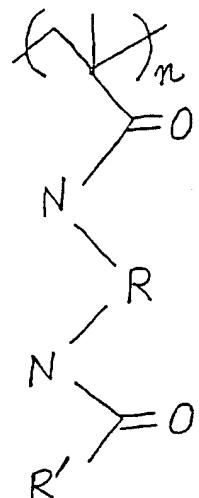
Group B:

5



or

10



wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a 15 divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group 20 having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, one or more hydroxyl groups and 3 to 9 carbon atoms; and n is 25 an integer of 2 or above; provided that when R represents an methylene group (-CH₂-), R' represents a hydroxymethyl group (-CH₂-OH) or a hydroxyethyl group (-CH₂CH₂-OH).

24. The heat-responsive polymer material as claimed in

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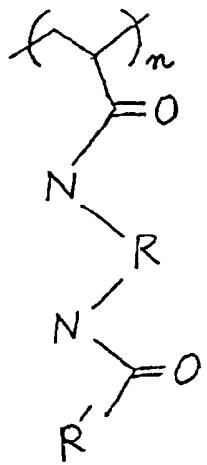
Claim 23, wherein said polymer compound has acid amide bonds at two or more sites in the polymer side chain.

25. The heat-responsive polymer material as claimed in
Claim 23 or 24 the polarity of the hydrophilic
nature/hydrophobic nature of which varies at its cloud point and
the polarity of which can be controlled depending on the pH value,
5 salt concentration or the size of R and R'.

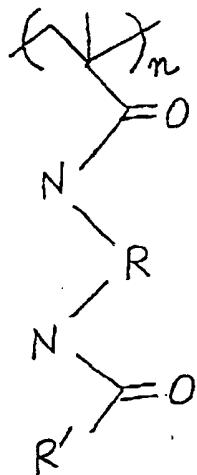
26. A Chromatographic packing which contains a polymer
compound represented by the following formula and shows a cloud
point due to a temperature change in an aqueous solution:

10 Group B:

15



or



20

wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms;
25 R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group

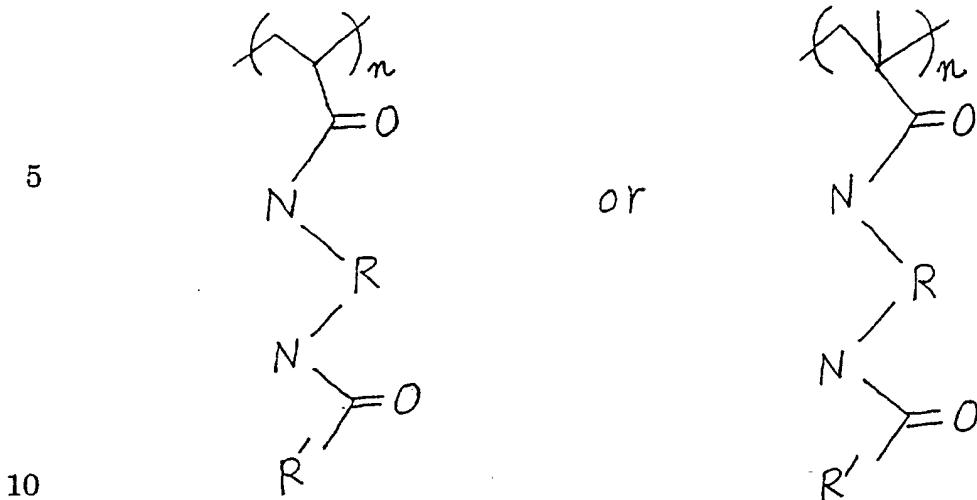
8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds,
5 one or more hydroxyl groups and 3 to 9 carbon atoms; and n is an integer of 2 or above; provided that when R represents an methylene group (-CH₂-), R' represents a hydroxymethyl group (-CH₂-OH) or a hydroxyethyl group (-CH₂CH₂-OH).

10 27. A chromatographic packing as claimed in Claim 26, wherein said polymer compound has acid amide bonds at two or more sites in the polymer side chain.

28. A method for separating substances characterized by
15 comprising holding a substance on a stationary phase comprising the chromatographic packing as claimed in Claim 25, then changing the hydrophilic/hydrophobic balance of the surface of the stationary phase by the temperature gradient method wherein the external temperature is changed stepwise, and then passing
20 through a single mobile phase, thus effecting separation.

29. (amended) A process for producing a polymer compound represented by the following formula:

Group B:



wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a 15 divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group 20 having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, one or more hydroxyl groups and 3 to 9 carbon atoms; and n is 25 an integer of 2 or above; provided that when R represents a methylene group (-CH₂-), R' represents a hydroxymethyl group (-CH₂-OH) or a hydroxyethyl group (-CH₂CH₂-OH); characterized by using one of the following methods:

- (1) reacting a compound selected from among aminoalkyl

acrylamide, aminoalkyl methacrylamide, aminoalkyl acrylamide hydrochloride and aminoalkyl methacrylamide hydrochloride with

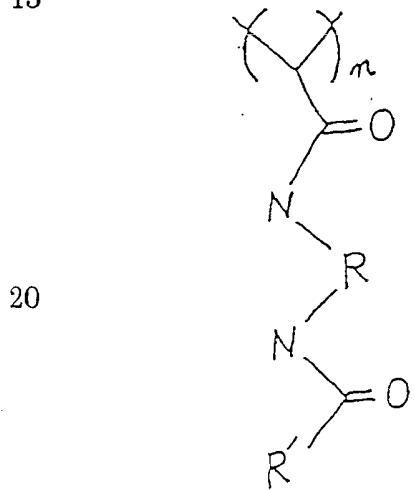
an acid anhydride or lactone, and purifying the thus obtained product followed by polymerization in a solvent; and

(2) reacting an alkyl diamine with an acid anhydride, an alkyl acid chloride or di-t-butyl dicarbonate, or reacting a 5 compound having an amino group and an amide bond in its molecule with acryloyl chloride or methacryloyl chloride, and then purifying the thus obtained product followed by polymerization in a solvent.

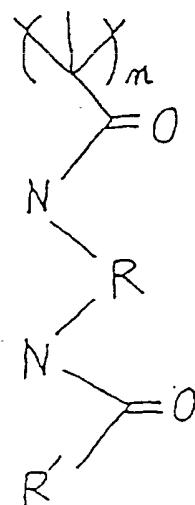
10 30. (amended) A material for separating or adsorbing biological samples which is a polymer compound represented by the following formula and has acid amide bonds at two or more sites in the polymer side chain:

Group B:

15



or



20

25 wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms;

R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group
5 having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, one or more hydroxyl groups and 3 to 9 carbon atoms; and n is an integer of 2 or above; provided that when R represents an
10 methylene group (-CH₂-), R' represents a hydroxymethyl group (-CH₂-OH) or a hydroxyethyl group (-CH₂CH₂-OH).

31. The material for separating or adsorbing biological samples as claimed in Claim 30 which has a functional group at
15 the polymer chain terminal.

32. The material for separating or adsorbing biological samples as claimed in Claim 31, wherein said functional group is selected from the group consisting of carboxyl, amino and
20 hydroxyl groups.

33. (amended) A method for separating substances characterized by comprising holding a biological sample on a stationary phase, then changing the hydrophilic/hydrophobic balance by changing the external temperature and thus adsorbing and separating the biological sample such as cells, wherein said stationary phase contains a polymer compound represented by the following formula and having acid amide bonds at two or more

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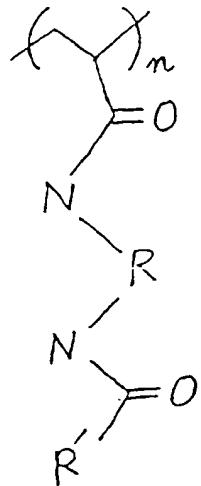
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side chain:

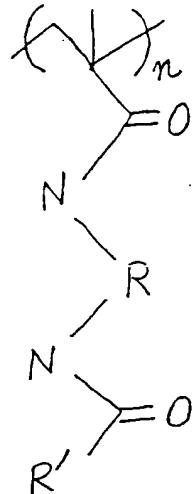
Group B:

5

10



or



wherein R represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms, or a 15 divalent aromatic hydrocarbon group having 6 to 14 carbon atoms; R' represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having one or more hydroxyl groups and 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group 20 having one or more acid amide bonds and/or ester bonds and 2 to 9 carbon atoms, or a linear or branched aliphatic hydrocarbon group having one or more acid amide bonds and/or ester bonds, one or more hydroxyl groups and 3 to 9 carbon atoms; and n is 25 an integer of 2 or above; provided that when R represents an methylene group (-CH₂-), R' represents a hydroxymethyl group (-CH₂-OH) or a hydroxyethyl group (-CH₂CH₂-OH).

34. The method for separating substances as claimed in

Claim 33, wherein said polymer compound has a functional group at the polymer chain terminal.

35. The method for separating substances as claimed in Claim 34, wherein said functional group is selected from the group consisting of carboxyl, amino and hydroxyl groups.

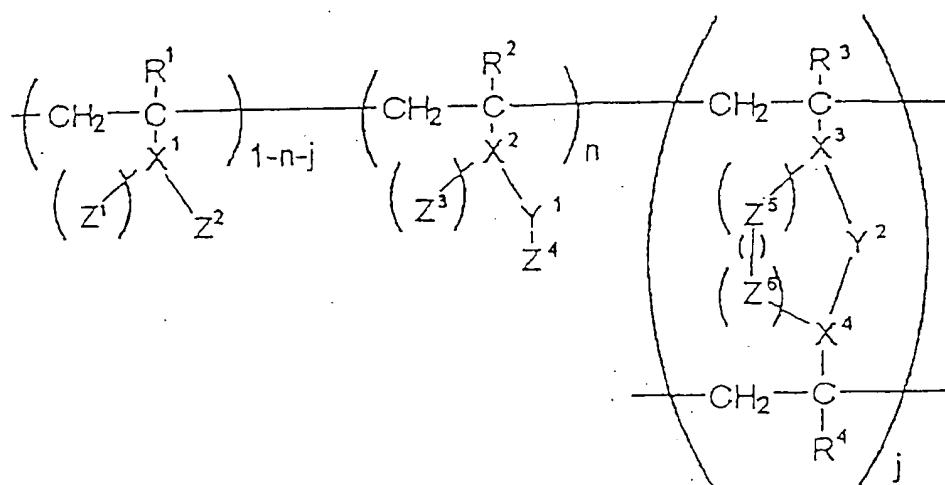
5 36. (amended) The polymer compound as claimed in Claim 1 which is selected from the group consisting of polymers containing a repeating unit represented by the following formula and crosslinked matters containing these polymers:

Group C-1:

10

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20



25

wherein n is the number of the middle kind of monomer unit, j is the number of the right kind of monomer unit, n is from 0.005 to 0.995 (inclusive) and j is from 0 to 0.5 (inclusive); R¹, R², R³ and R⁴ are the same or different and each represents a hydrogen atom or a methyl group; X¹, X², X³ and X⁴ are the same or different and each represents an acid amide group, an ester group or an ether group; Y¹ represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms, a

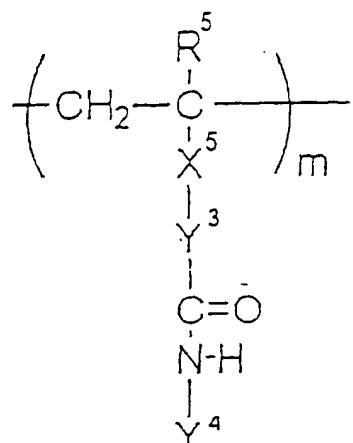
hydrocarbon group having 1 to 8 carbon atoms and one or more carbonyl groups, a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more nitryl groups, or a linear or branched aliphatic hydrocarbon group having 1 to 5 8 carbon atoms and one or more hydroxyl groups; provided that when X¹ represents an acid amide group, either Z¹ or Z² represents a hydrogen atom or a glycoside having 3 to 12 carbon atoms, provided that neither Z¹ nor Z² represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms or a 10 linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more hydroxyl groups, and provided that when Y¹ represents a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms and Z⁴ represents a aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more amide groups, 15 X² represents an acid amide group.

37. The polymer compound as claimed in claim 36 characterized by containing an aromatic hydrocarbon group.

20 38. The polymer compound as claimed in claim 1 comprising a polymer represented by the following formula:

Group C-2:

5



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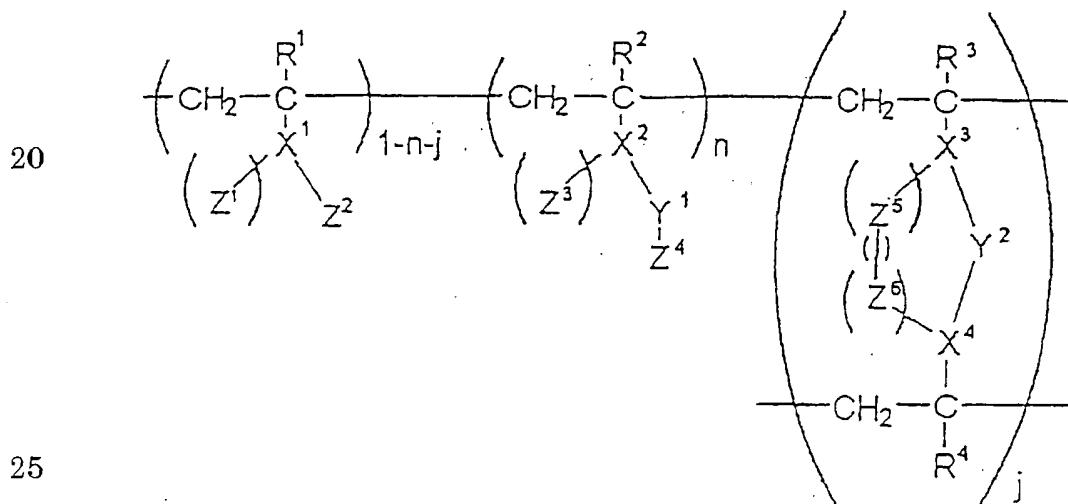
wherein R⁵ represents a hydrogen atom or a methyl group; X⁵ represents an acid amide group, an ester group or an ether group; Y³ represents a linear or branched divalent aliphatic hydrocarbon group having 1 to 8 carbon atoms or a divalent alicyclic hydrocarbon group having 3 to 8 carbon atoms; and Y⁴ represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms or a linear or branched aliphatic

hydrocarbon group having 1 to 8 carbon atoms and one or more hydroxyl groups.

39. The polymer compound as claimed in claim 36 or 38
5 characterized in that said repeating unit of the polymer contains two or more amide or ester groups which are either the same or different.

40. (amended) A temperature-responsive polymer compound
10 which is a polymer compound selected from the group consisting of polymers containing a repeating unit represented by the following formula and crosslinked matters containing these polymers, characterized by expressing a temperature-responsiveness of changing its characteristics under a
15 temperature change:

Group C-1:



wherein n is the number of the middle kind of monomer unit, j

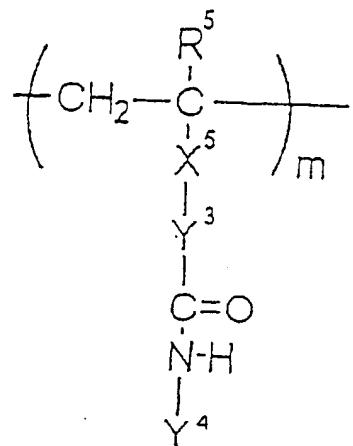
Z^6 are functional groups bonded respectively to X^1 , X^2 , X^3 and X^4 when they are tertiary amide groups and Z^5 may be bonded to Z^6 ; and Z^4 represents a hydrogen atom, a hydroxyl group, an amide group, a nitryl group, a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more amide groups, a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more carbonyl groups, a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more nitryl groups, or a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more hydroxyl groups; provided that when X^1 represents an acid amide group, either Z^1 or Z^2 represents a hydrogen atom or a glycoside having 3 to 12 carbon atoms, provided that neither Z^1 nor Z^2 represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms or a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more hydroxyl groups, and provided that when Y^1 represents a divalent aromatic hydrocarbon group having 6 to 14 carbon atoms and Z^4 represents a aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more amide groups, X^2 represents an acid amide group.

41. A temperature-responsive polymer compound which is
25 a polymer compound comprising a polymer represented by the following formula, characterized by expressing a temperature-responsiveness of changing its characteristics under a temperature change:

Group C-2:

5

10

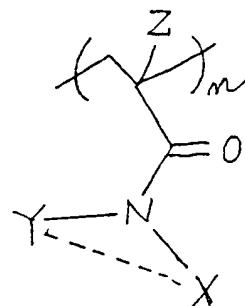


claimed in claim 40 or 41.

46. (amended) The polymer compound as claimed in claim 1 containing a repeating unit represented by the following formula (I) and showing temperature-responsiveness in a solution:

Group D:

10



15

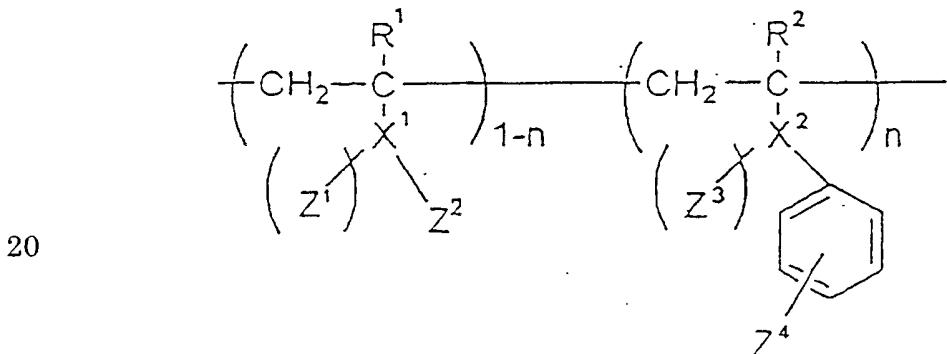
wherein Z represents a hydrogen atom or a methyl group; X represents a hydrogen atom or a cyclic hydrocarbon group having 3 to 8 carbon atom and carrying at least one hydroxyl group; Y represents a cyclic hydrocarbon group having 3 to 8 carbon atom 20 and carrying at least one hydroxyl group, or X and Y may form together a chemical bond; and n is an integer of 2 or.

47. The polymer compound as claimed in claim 46, wherein the monomer represented by Group D is a compound synthesized by 25 reacting acrylic acid chloride, methacrylic acid chloride, anhydrous acrylic acid or anhydrous methacrylic acid with an alkylamino alcohol.

temperature) of which can be controlled in an aqueous solution system depending on the size of the side chain R, salt concentration, pH value, polymer concentration, polymer density, organic solvent concentration, the composition of a homopolymer or a copolymer with another polymerizable monomer and polymer molecular weight.

88. (amended) The temperature-responsive polymer compound as claimed in claim 1 which is selected from the group consisting of polymers containing a repeating unit represented by the following formula and crosslinked matters containing these polymers, characterized in that the temperature-responsiveness thereof is controlled by changing the salt concentration in a solution:

15 Group E-5:



wherein n is n is the number of the right kind of monomer unit compared to the total number of the two kinds of monomer units shown and is an arbitrary value falling within the range 0.005 ≤ n ≤ 0.995; R¹ and R² are the same or different and each represents a hydrogen atom or a methyl group; X¹ and X² are the

same or different and each represents an acid amide or ester group; Z¹, Z² and Z³ are the same or different and each represents a hydrogen atom, a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, a linear or branched hydrocarbon group having 1 to 8 carbon atoms and containing at least one hydroxyl group, a linear or branched hydrocarbon group having 1 to 8 carbon atoms and containing at least one ether group, a glycoside having 3 to 12 carbon atoms or a glycoside having 3 to 12 carbon atoms and containing a linear or branched hydrocarbon group having 1 to 8 carbon atoms, provided that Z¹ or Z³ is a functional group carried by X¹ or X² which is a tertiary amide; and Z⁴ represents a hydrogen atom, a hydroxyl group, an amide group, a linear or branched hydrocarbon group having 1 to 8 carbon atoms and containing at least one amide group, a linear or branched hydrocarbon group having 1 to 8 carbon atoms and containing at least one carbonyl group or a linear or branched hydrocarbon group having 1 to 8 carbon atoms and containing at least one hydroxyl group which may be attached at an arbitrary position, i.e., o-, m- or p-position; provided that when X¹ represents an acid amide group, either Z¹ or Z² represents a hydrogen atom or a glycoside having 3 to 12 carbon atoms, provided that neither Z¹ nor Z² represents a linear or branched aliphatic hydrocarbon group having 1 to 8 carbon atoms, and provided that when Z⁴ represents a aliphatic hydrocarbon group having 1 to 8 carbon atoms and one or more amide groups, X² represents an acid amide group.

89. A material for separation, adsorption or release of

substances whereby biological molecules, biological samples or substances can be adsorbed, released or separated, characterized by using the polymer material as claimed in any of claims 62 to 88.

5

90. A method for separating substances characterized by fixing the polymer material as claimed in claim 89 to a

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

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NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

<p>To:</p> <p>YUASA & HARA Attn. Tomita, Hiroyuki Section 206, New Otemachi Bldg, 2-1 Otemachi 2-chome Chiyoda-ku TOKYO 100-0004 JAPAN</p>	<p style="text-align: center;">PCT</p>
<p>Date of mailing (day/month/year) 28/06/2000</p>	
<p>Applicant's or agent's file reference YCT-469</p>	<p>FOR FURTHER ACTION See paragraphs 1 and 4 below</p>
<p>International application No. PCT/JP 00/00510</p>	<p>International filing date (day/month/year) 31/01/2000</p>
<p>Applicant AMERSHAM PHARMACIA BIOTECH K.K. et al.</p>	

1. The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland
 Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

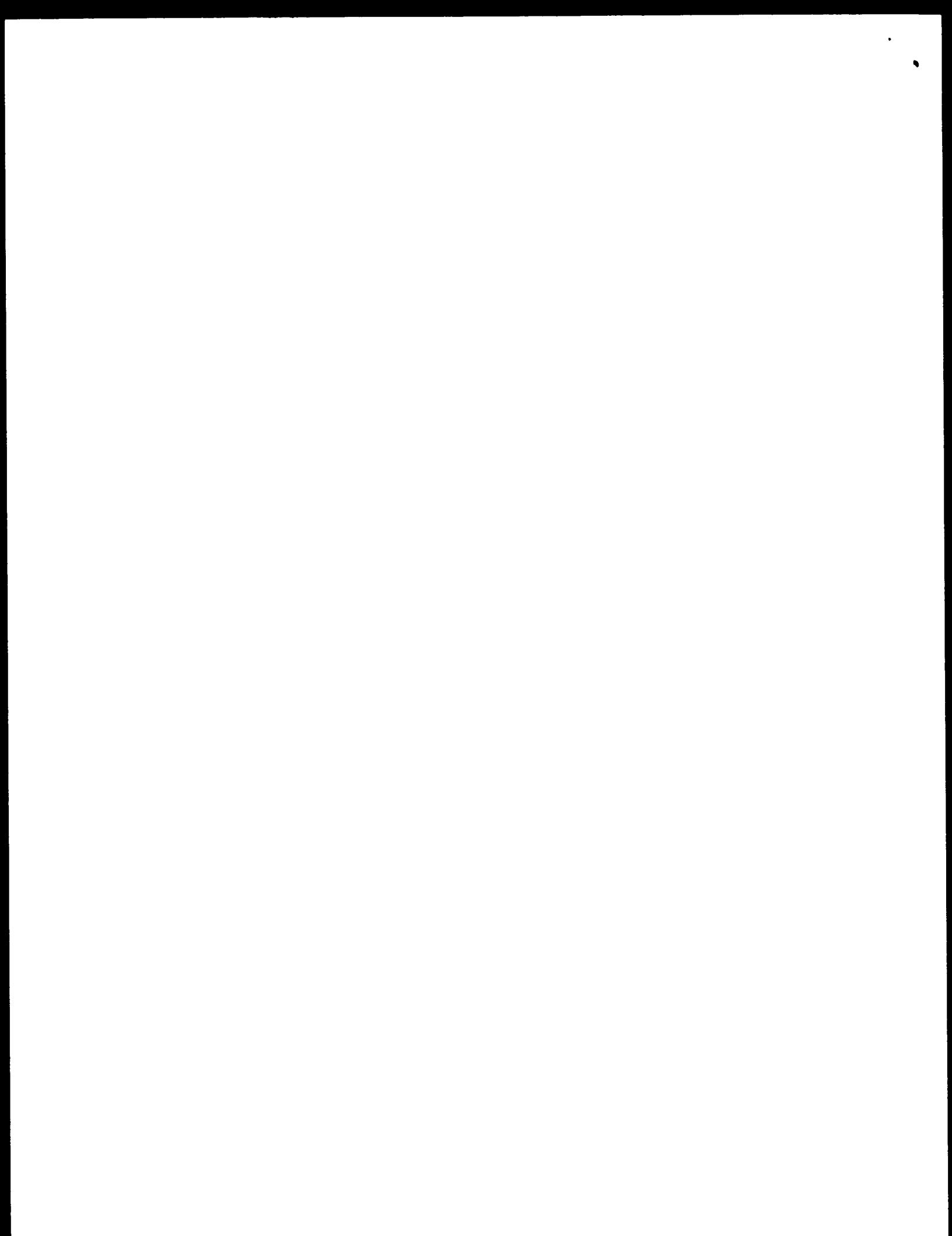
4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

<p>Name and mailing address of the International Searching Authority</p> <p>European Patent Office, P.B. 5818 Patentdaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016</p>	<p>Authorized officer</p> <p>Philip Van Kalsbeek</p>
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NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

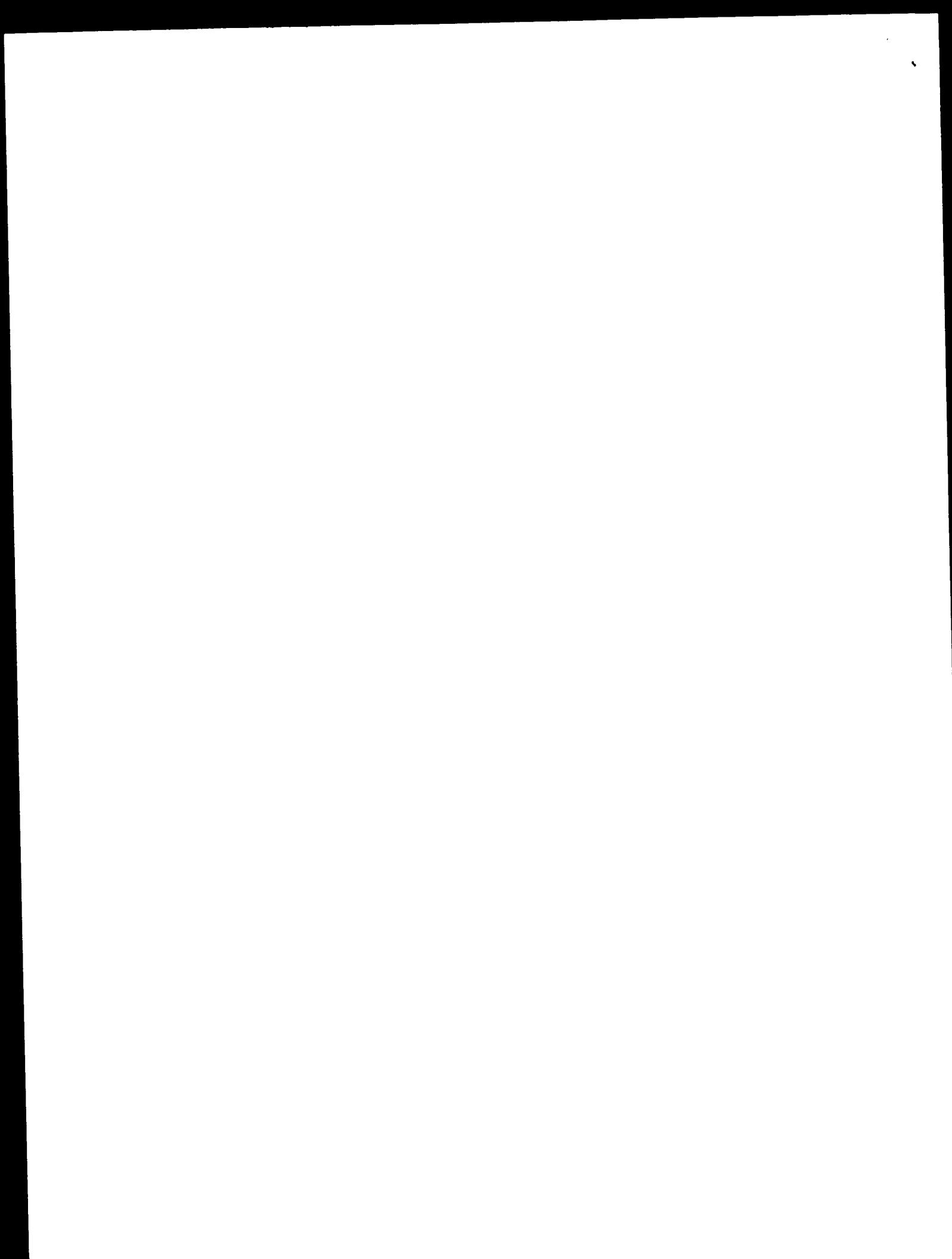
What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.



NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

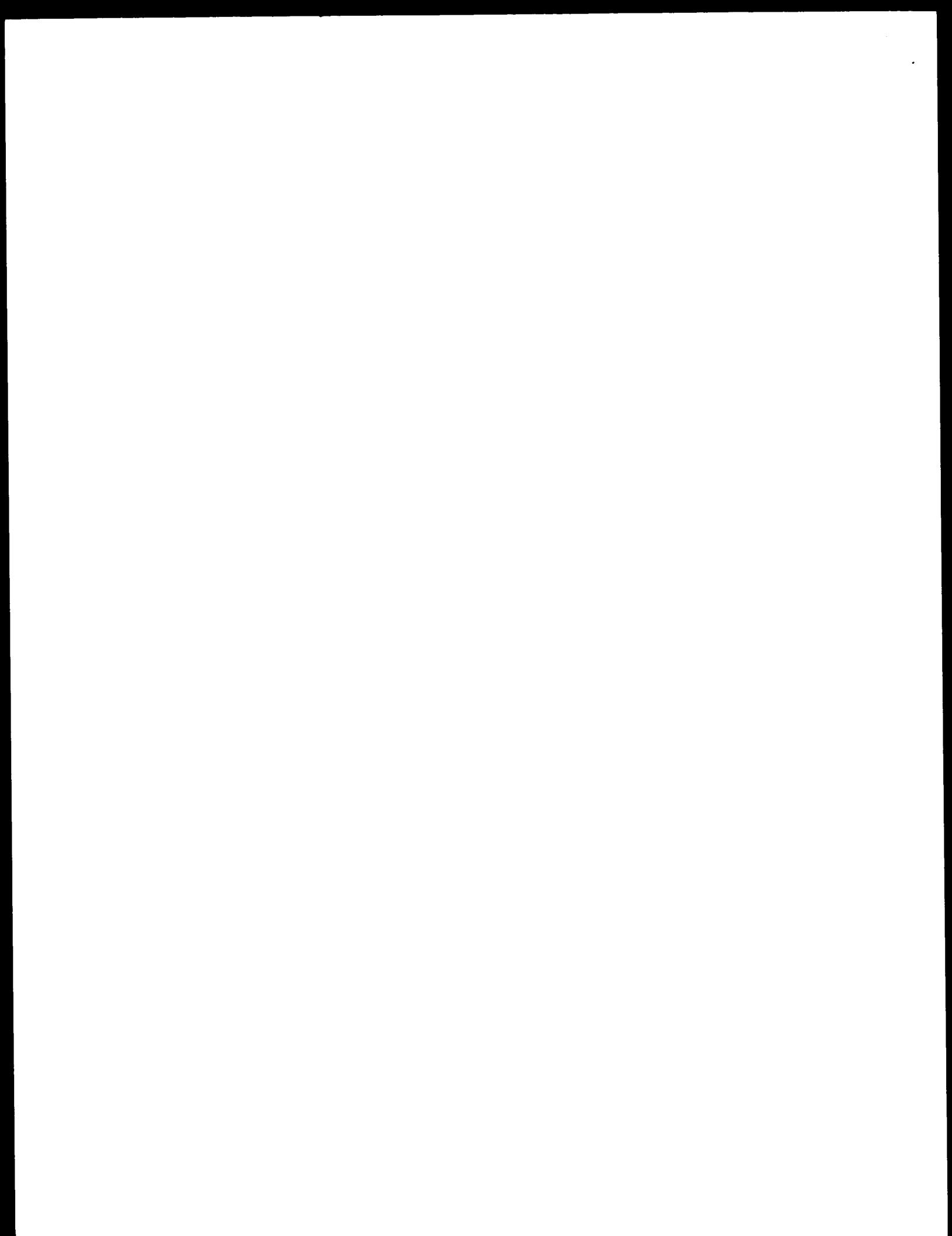
Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence)

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide



PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference YCT-469	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/JP 00/00510	International filing date (day/month/year) 31/01/2000	(Earliest) Priority Date (day/month/year) 29/01/1999
Applicant AMERSHAM PHARMACIA BIOTECH K.K. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :
 - contained in the international application in written form.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority in written form.
 - furnished subsequently to this Authority in computer readable form.
 - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. Certain claims were found unsearchable (See Box I).

3. Unity of Invention is lacking (see Box II).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

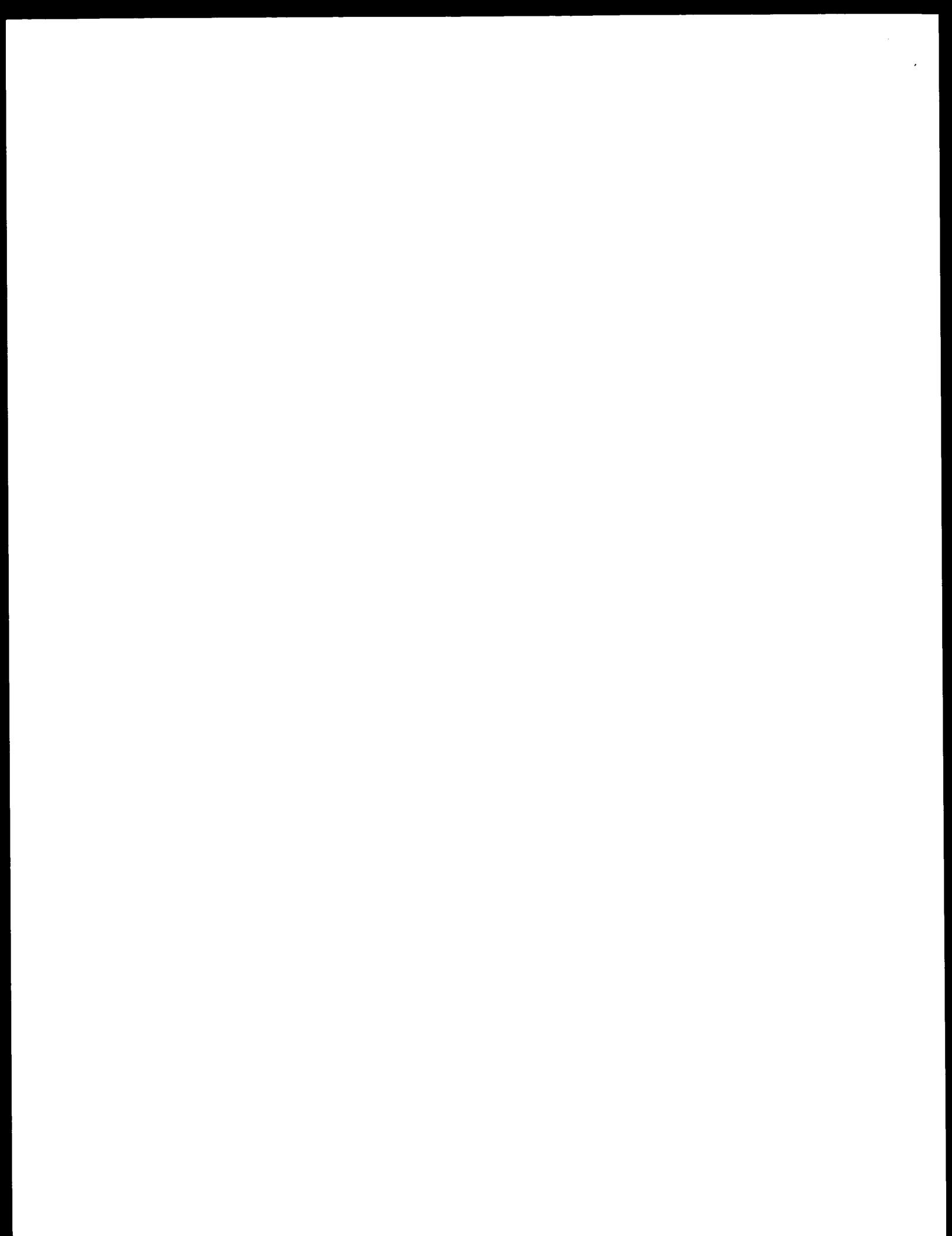
5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. _____

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.



INTERNATIONAL SEARCH REPORT

International Application No
PCT/JP 00/00510

A. CLASSIFICATION OF SUBJECT MATTER	IPC 7 C08F20/36	C08F20/28	C08F20/58
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C08F20/60	G01N30/48
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C08F G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2 458 420 A (EASTMAN KODAK COMPANY) 4 January 1949 (1949-01-04) claims 1,5 column 1, line 54 -column 2, line 31	1-4, 12, 38 6-8, 41, 44
A	EP 0 970 945 A (DSM NV) 12 January 2000 (2000-01-12) claims 1,5 page 3	1-4 6, 12
A	EP 0 697 400 A (NIPPON PAINT CO LTD) 21 February 1996 (1996-02-21) page 3, line 37-50	1, 12 -/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

16 May 2000

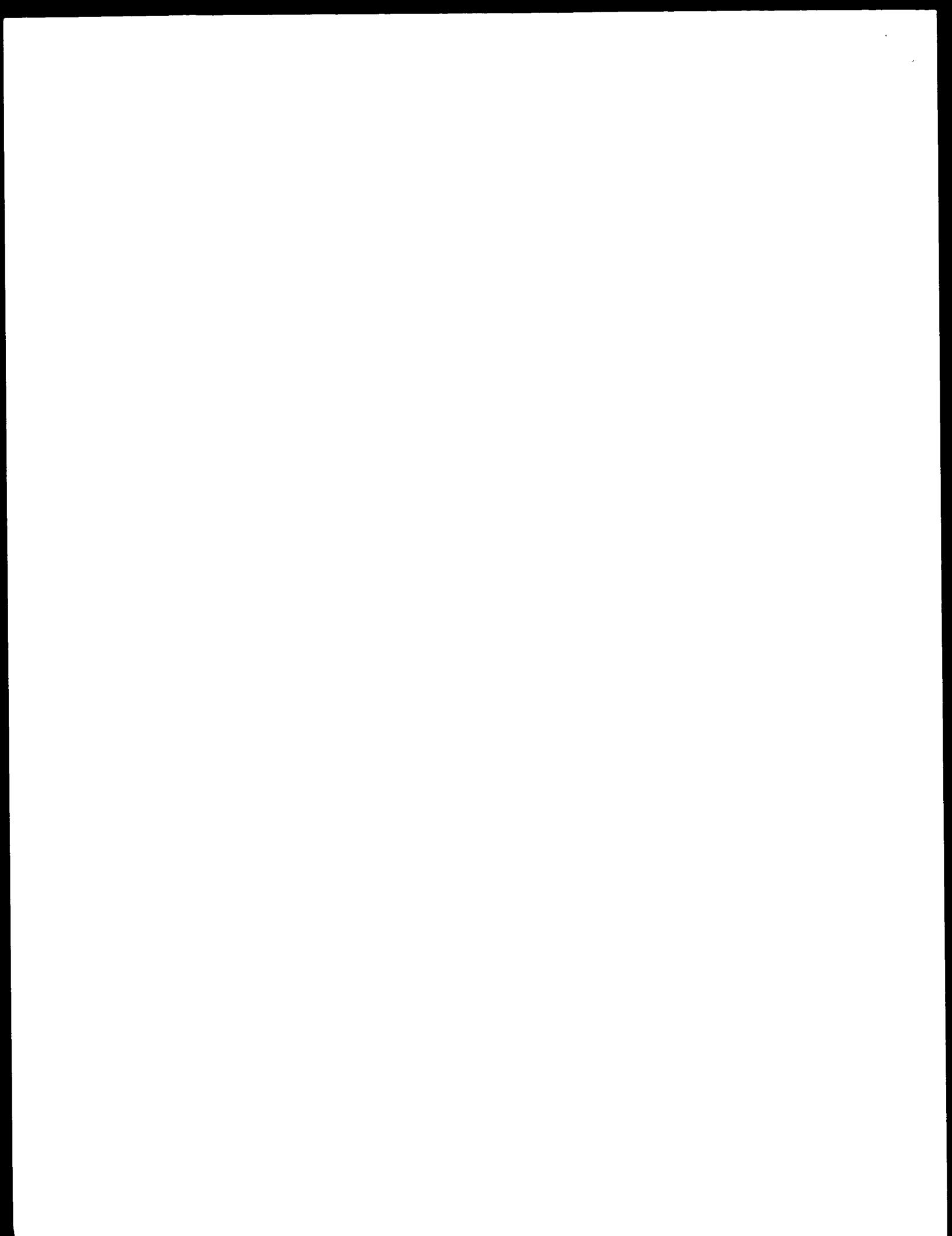
28/06/2000

Name and mailing address of the ISA

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NL - 2280 HV Rijswijk
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Fax: (+31-70) 340-3016

Authorized officer

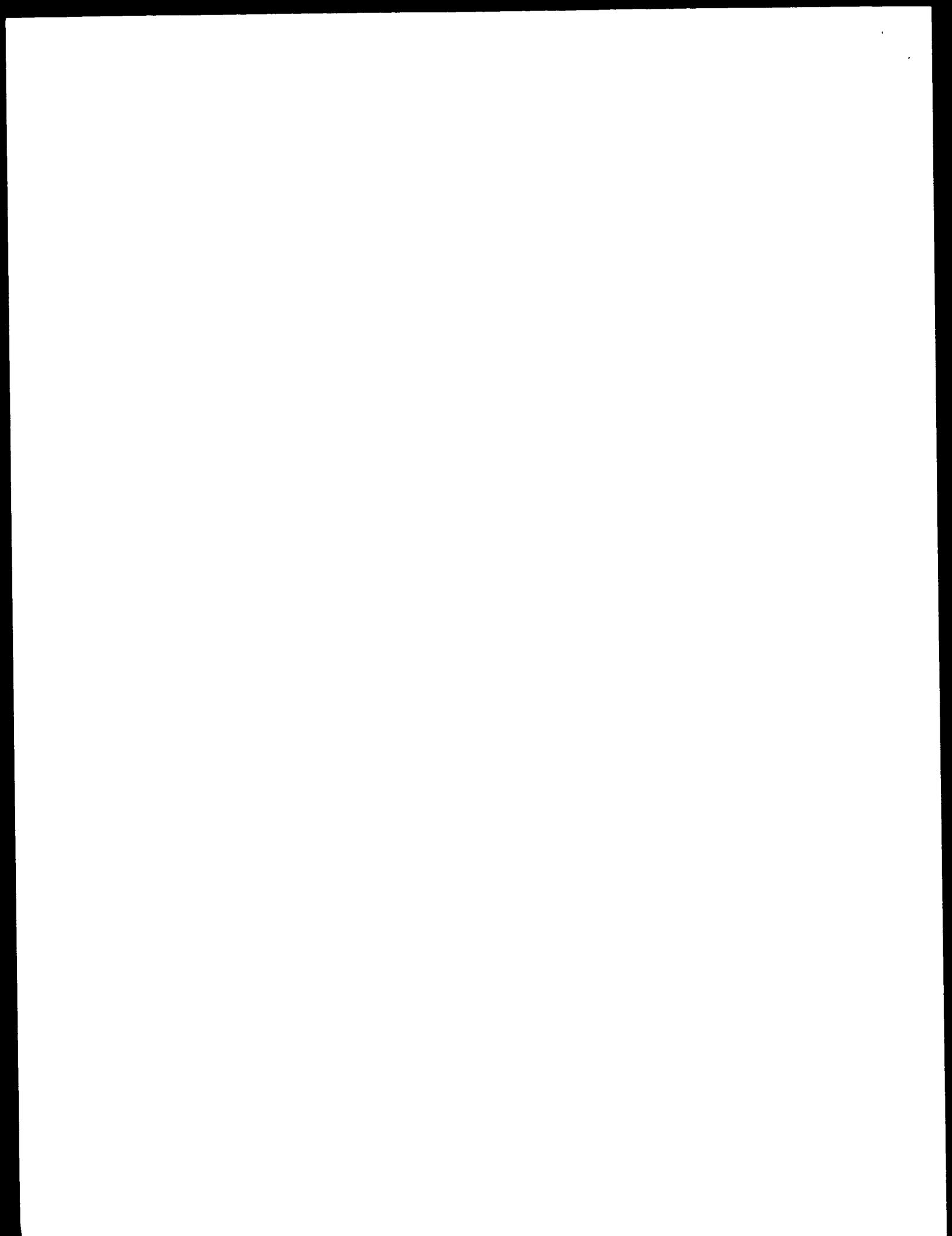
Rose, E



INTERNATIONAL SEARCH REPORT

International Application No
PCT/JP 00/00510

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 969 436 A (WICHTERLE OTTO ET AL) 13 July 1976 (1976-07-13) column 1, line 28,29 column 2, line 39,40 column 2, line 59-67 ---	1-18
A	EP 0 394 787 A (BAYER AG) 31 October 1990 (1990-10-31) page 25, line 53 -page 26, line 9 ---	12
X	US 3 721 565 A (FITZGERALD M) 20 March 1973 (1973-03-20) claim 1 column 17, line 13-20 column 18, line 56-59 ---	1,19,38
X	US 4 062 831 A (KOPECEK JINRICH ET AL) 13 December 1977 (1977-12-13) claims 1-5 examples 3,12 column 2, line 62 ---	1,36,37, 39-45
A	CHEMICAL ABSTRACTS, vol. 79, no. 22, 3 December 1973 (1973-12-03) Columbus, Ohio, US; abstract no. 126818, YAKOVLEVA, M. K. ET AL: "Radiation polymerization of acrylamide in two-phase systems" XP002137858 abstract & RADIATS. KHIM. (1972), 2, 251-7 FROM: REF. ZH., KHIM. 1973, ABSTR. NO. 3S154, ---	1,36
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E	WO 00 07002 A (BIOWHITTAKER MOLECULAR APPLIC) 10 February 2000 (2000-02-10) example 1 claim 1 ---	1,46-53
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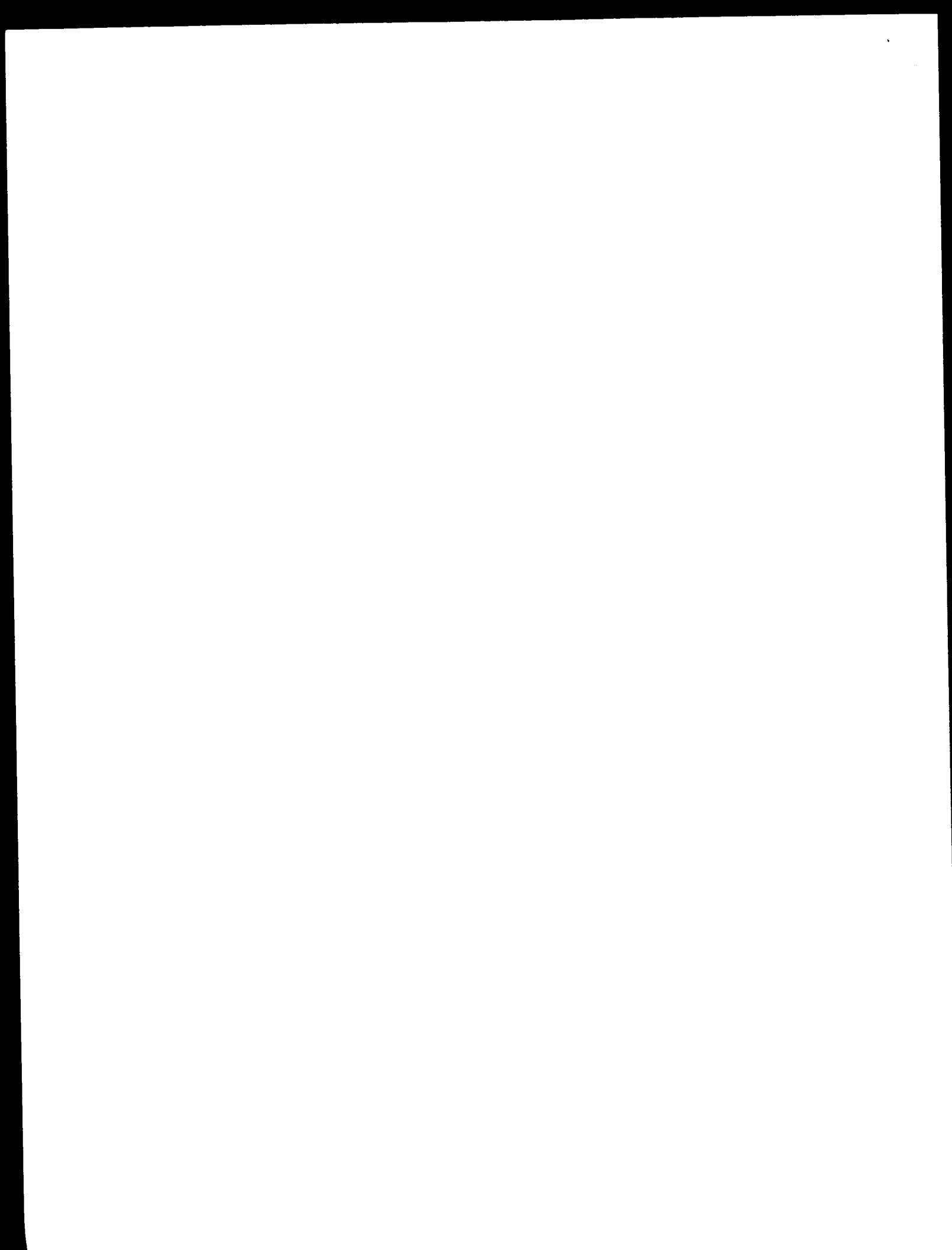
INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 00/00510

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHEMICAL ABSTRACTS, vol. 125, no. 20, 11 November 1996 (1996-11-11) Columbus, Ohio, US; abstract no. 256962, OGATA, NAOYA: "Applications of temperature-responsive polymers for drug delivery systems" XP002137584 abstract & POLYM. PREPR. (AM. CHEM. SOC., DIV. POLYM. CHEM.) (1996), 37(2), 113-114 , ----	1,46-53, 61
A	MICEWICZ, BEATA ET AL: "Mechanism of tyrosine fluorescence quenching by acrylamide in model peptides" , PEPT. 1996, PROC. EUR. PEPT. SYMP., 24TH (1998), MEETING DATE 1996, 649-650. EDITOR(S): RAMAGE, ROBERT; EPTON, ROGER. PUBLISHER: MAYFLOWER SCIENTIFIC, KINGSWINFORD, UK. XP000907133 ----	1,62
X	GB 1 409 967 A (CESKOSLOVENSKA AKADEMIE VED) 15 October 1975 (1975-10-15)	1,88,89
A	claim 1 column 3, line 45,46 -----	90



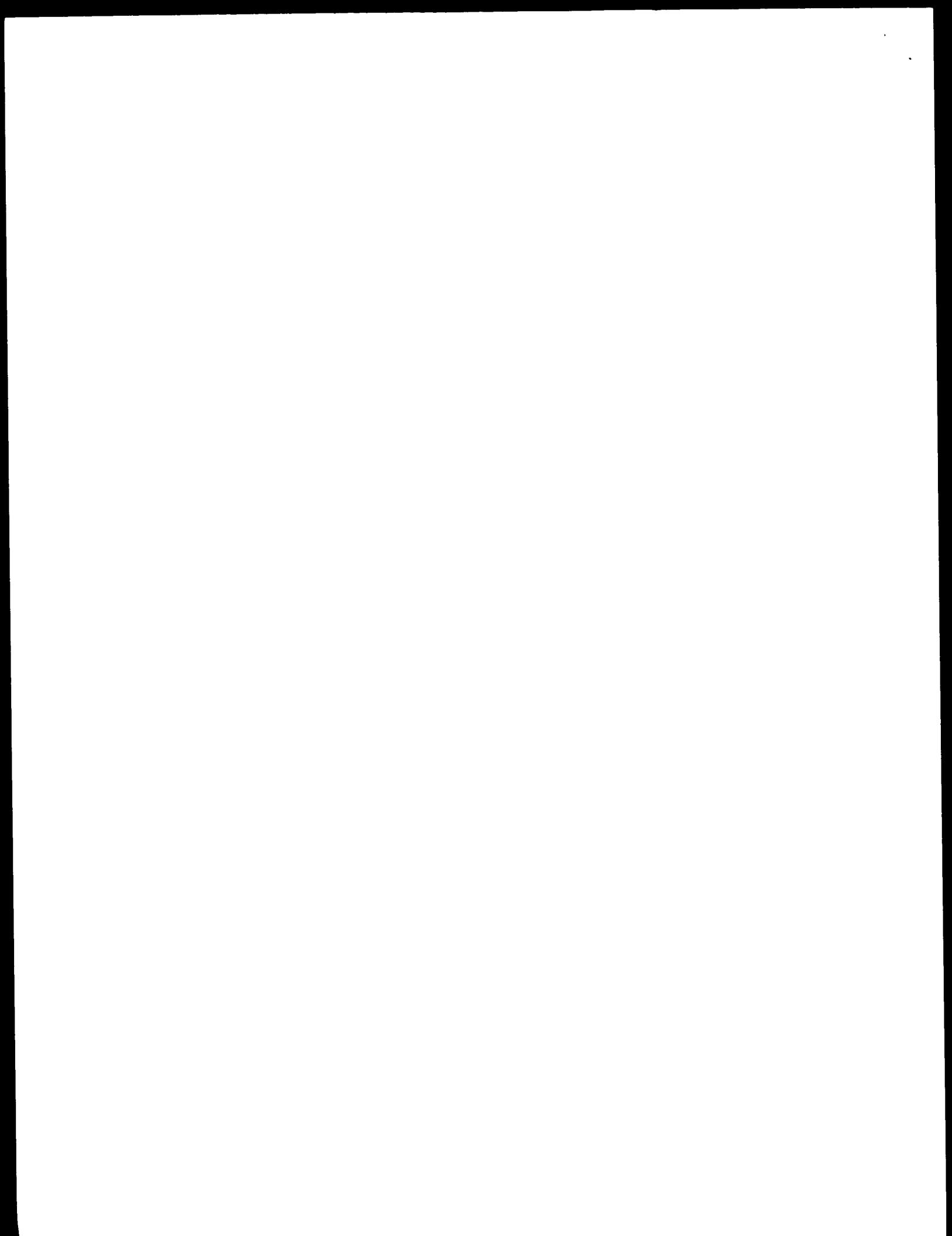
INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 00/00510

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US 2458420	A	04-01-1949	NONE		
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WO 0007002	A	10-02-2000	NONE		



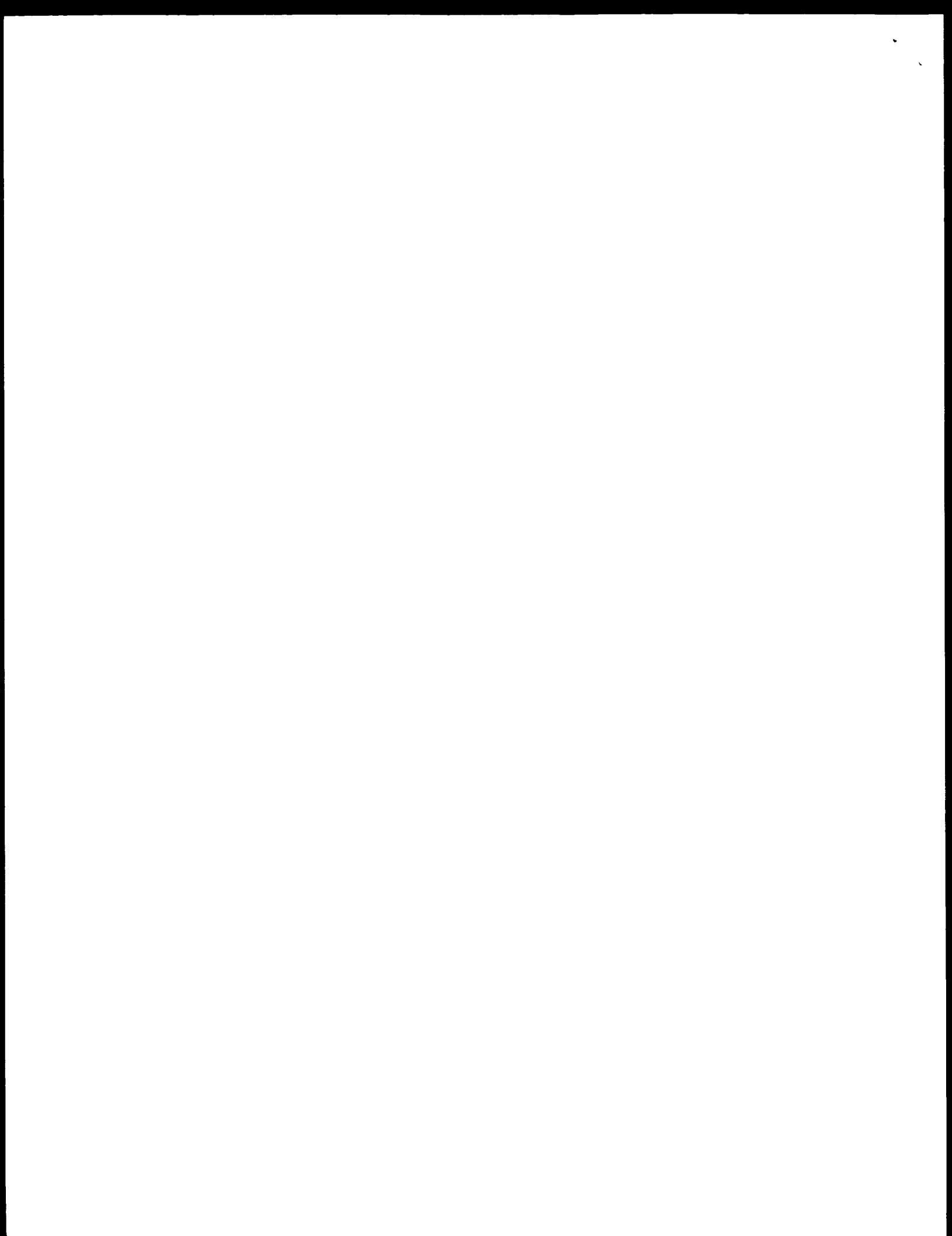
INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 00/00510

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
GB 1409967	A 15-10-1975	CS	166317 B	27-02-1976
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		SE	388204 B	27-09-1976
		US	4076691 A	28-02-1978



PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

Date of mailing (day/month/year) 24 August 2000 (24.08.00)	To: Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ETATS-UNIS D'AMERIQUE in its capacity as elected Office
International application No. PCT/JPO0/00510	Applicant's or agent's file reference YCT-469
International filing date (day/month/year) 31 January 2000 (31.01.00)	Priority date (day/month/year) 29 January 1999 (29.01.99)
Applicant AKIYAMA, Yoshikatsu et al	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

10 July 2000 (10.07.00)

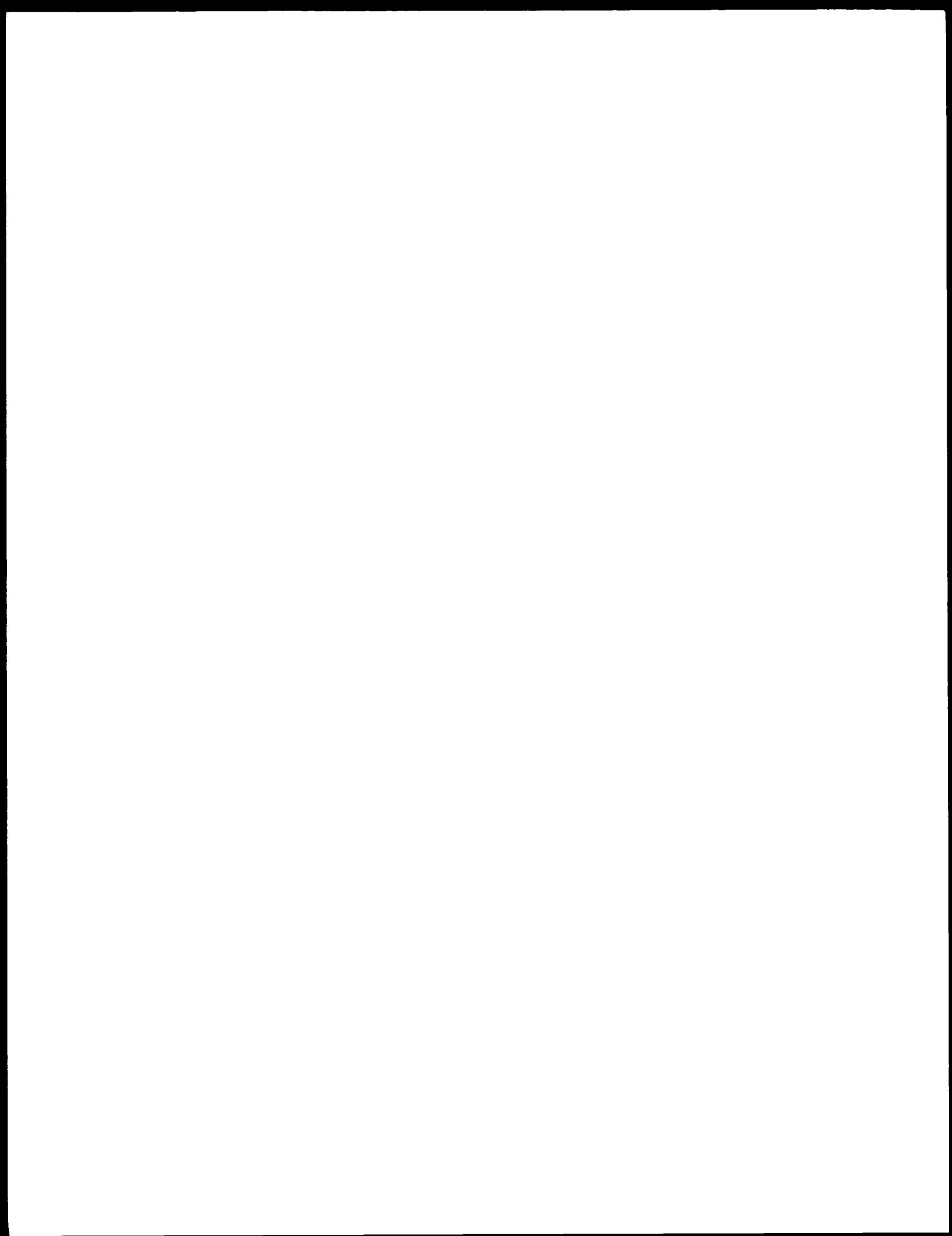
in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Henrik Nyberg Telephone No.: (41-22) 338.83.38
---	---



PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference YCT-469	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/JP 00/00510	International filing date (day/month/year) 31/01/2000	(Earliest) Priority Date (day/month/year) 29/01/1999
Applicant AMERSHAM PHARMACIA BIOTECH K.K. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:
 - contained in the international application in written form.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority in written form.
 - furnished subsequently to this Authority in computer readable form.
 - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. **Certain claims were found unsearchable** (See Box I).

3. **Unity of Invention Is lacking** (see Box II).

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

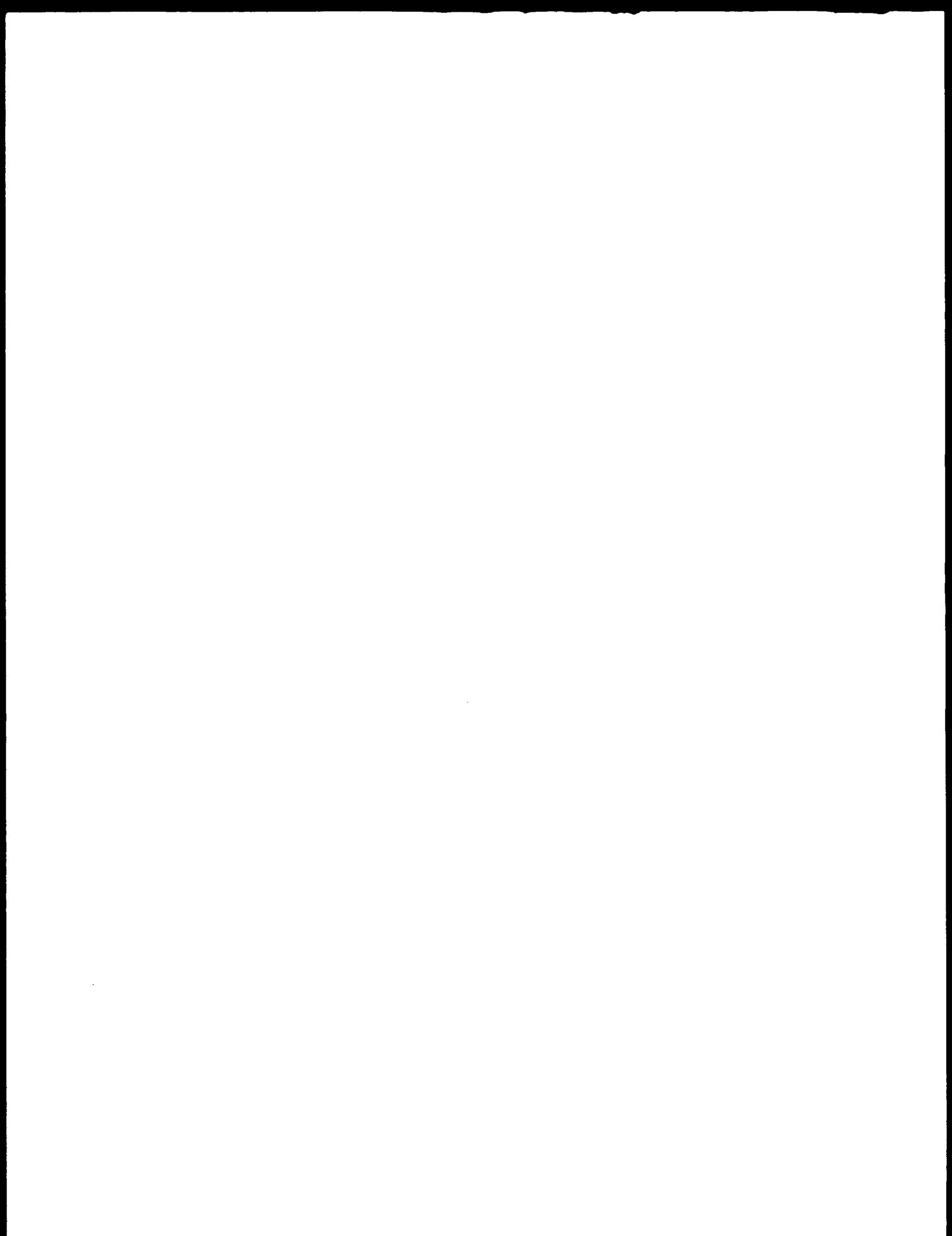
5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. ---

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.



INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 00/00510

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C08F20/36 C08F20/28 C08F20/58 C08F20/60 G01N30/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C08F G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2 458 420 A (EASTMAN KODAK COMPANY) 4 January 1949 (1949-01-04) A claims 1,5 column 1, line 54 -column 2, line 31 ---	1-4,12, 38 6-8,41, 44
P,X	EP 0 970 945 A (DSM NV) 12 January 2000 (2000-01-12) A claims 1,5 page 3 ---	1-4
A	EP 0 697 400 A (NIPPON PAINT CO LTD) 21 February 1996 (1996-02-21) A page 3, line 37-50 ---	6,12
A		1,12 -/--

Further documents are listed in the continuation of box C.

Patent family members are listed in annex

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

16 May 2000

Date of mailing of the international search report

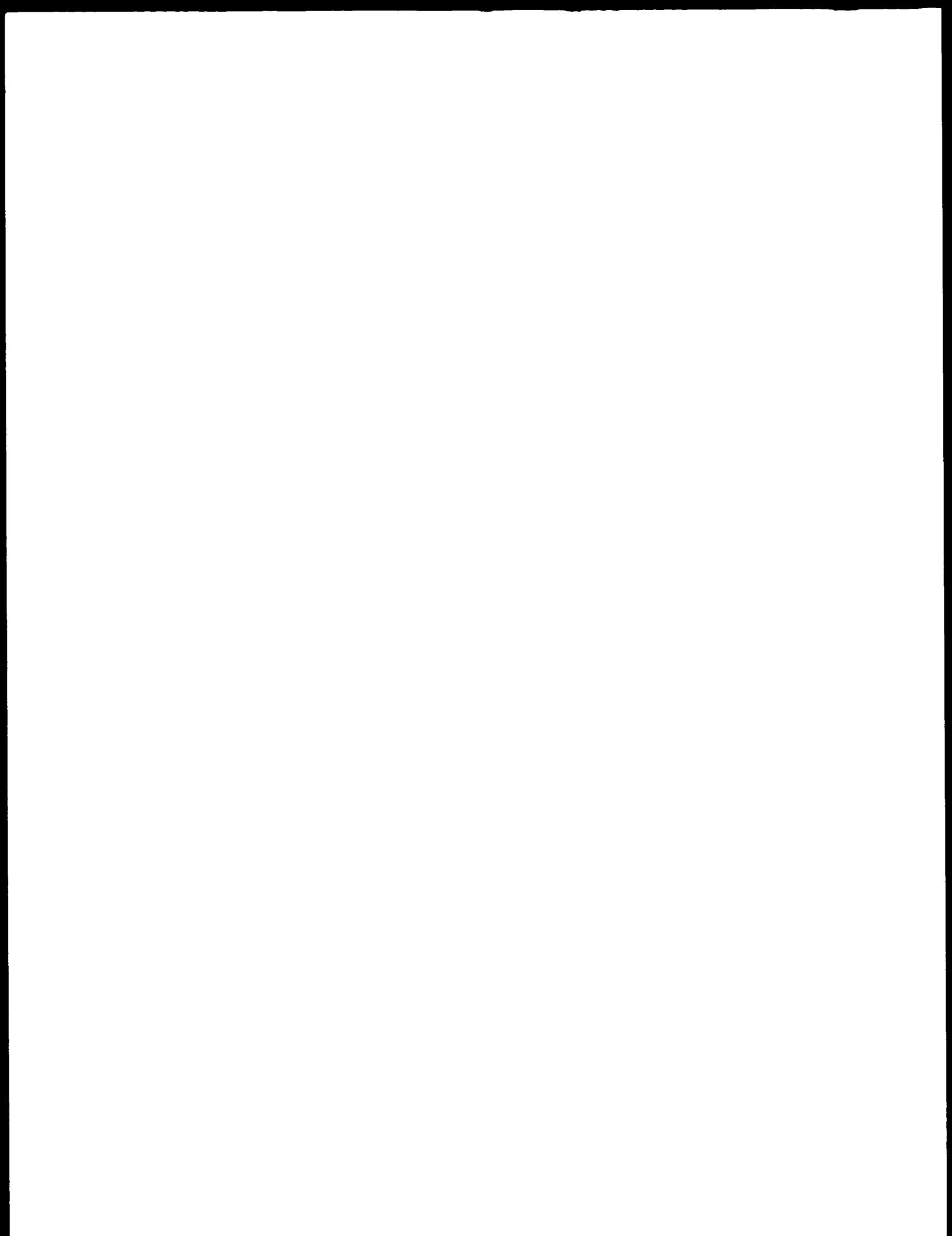
28/06/2000

Name and mailing address of the ISA

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Fax: (+31-70) 340-3016

Authorized officer

Rose, E

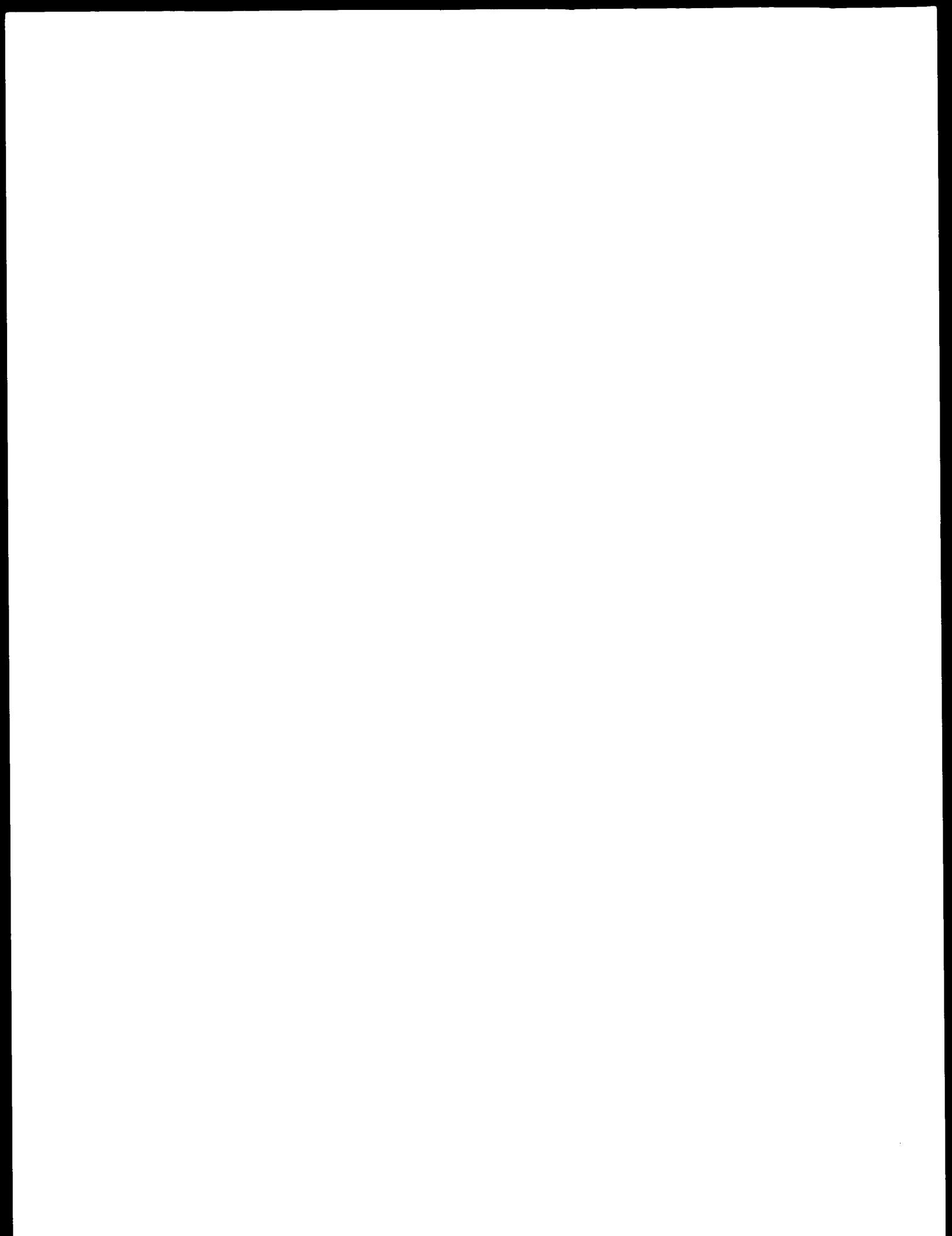


INTERNATIONAL SEARCH REPORT

International Application No PCT/JP 00/00510

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

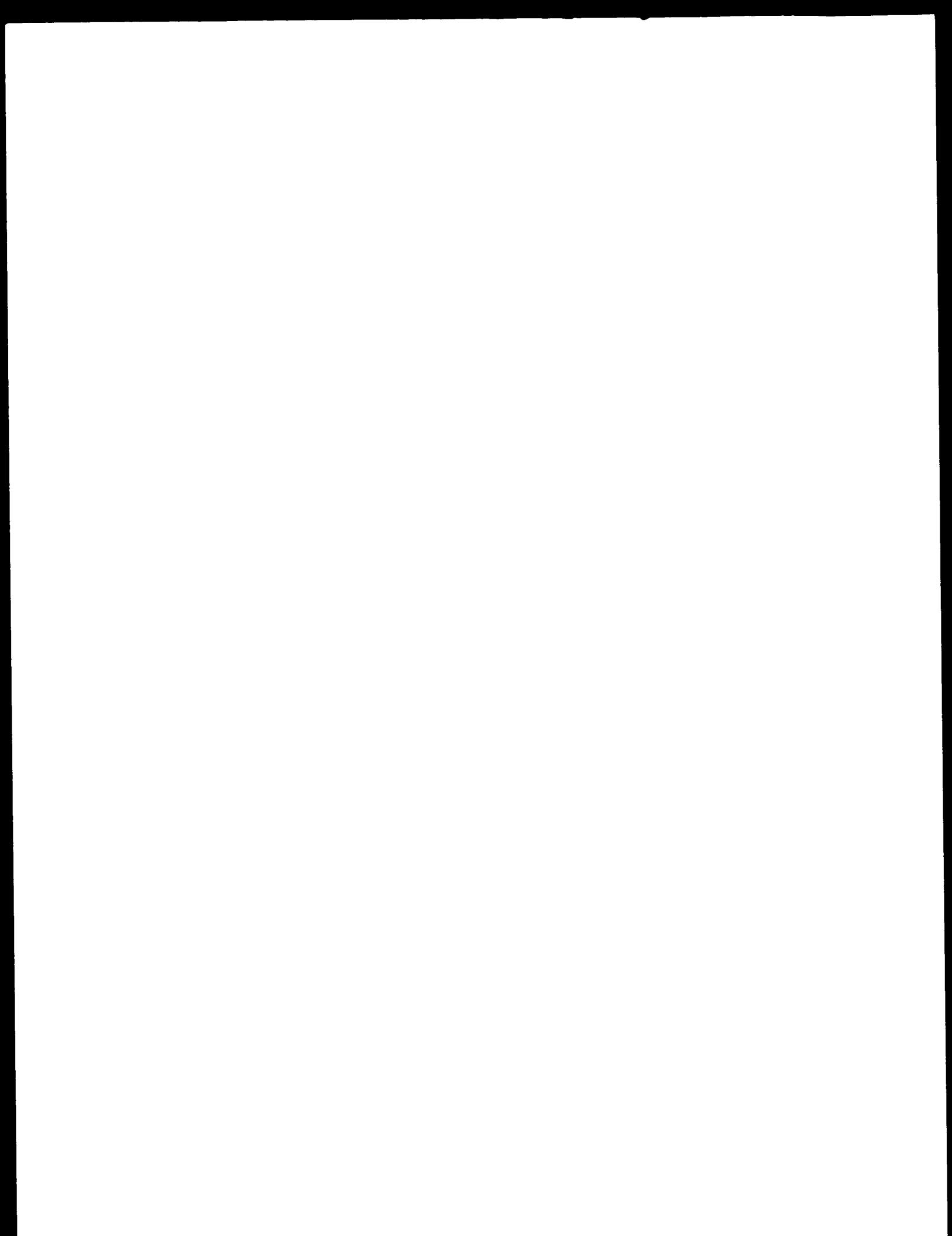
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 969 436 A (WICHTERLE OTTO ET AL) 13 July 1976 (1976-07-13) column 1, line 28,29 column 2, line 39,40 column 2, line 59-67 ---	1-18
A	EP 0 394 787 A (BAYER AG) 31 October 1990 (1990-10-31) page 25, line 53 -page 26, line 9 ---	12
X	US 3 721 565 A (FITZGERALD M) 20 March 1973 (1973-03-20) claim 1 column 17, line 13-20 column 18, line 56-59 ---	1, 19, 38
X	US 4 062 831 A (KOPECEK JINRICH ET AL) 13 December 1977 (1977-12-13) claims 1-5 examples 3,12 column 2, line 62 ---	1, 36, 37, 39-45
A	CHEMICAL ABSTRACTS, vol. 79, no. 22, 3 December 1973 (1973-12-03) Columbus, Ohio, US; abstract no. 126818, YAKOVLEVA, M. K. ET AL: "Radiation polymerization of acrylamide in two-phase systems" XP002137858 abstract & RADIATS. KHIM. (1972), 2, 251-7 FROM: REF. ZH., KHIM. 1973, ABSTR. NO. 3S154, ---	1, 36
X	DATABASE WPI Section Ch, Week 199440 Derwent Publications Ltd., London, GB; Class A41, AN 1994-322147 XP002137859 & JP 06 247917 A (NIPPON SHOKUBAI CO LTD), 6 September 1994 (1994-09-06) abstract ----	1, 38
E	WO 00 07002 A (BIOWHITTAKER MOLECULAR APPLIC) 10 February 2000 (2000-02-10) example 1 claim 1 ----	1, 46-53
		-/-



INTERNATIONAL SEARCH REPORT

International Application No PCT/JP 00/00510

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHEMICAL ABSTRACTS, vol. 125, no. 20, 11 November 1996 (1996-11-11) Columbus, Ohio, US; abstract no. 256962, OGATA, NAOYA: "Applications of temperature-responsive polymers for drug delivery systems" XP002137584 abstract & POLYM. PREPR. (AM. CHEM. SOC., DIV. POLYM. CHEM.) (1996), 37(2), 113-114 , ----	1,46-53, 61
A	MICEWICZ, BEATA ET AL: "Mechanism of tyrosine fluorescence quenching by acrylamide in model peptides" , PEPT. 1996, PROC. EUR. PEPT. SYMP., 24TH (1998), MEETING DATE 1996, 649-650. EDITOR(S): RAMAGE, ROBERT;EPTON, ROGER. PUBLISHER: MAYFLOWER SCIENTIFIC, KINGSWINFORD, UK. XP000907133 ----	1,62
X	GB 1 409 967 A (CESKOSLOVENSKA AKADEMIE VED) 15 October 1975 (1975-10-15)	1,88,89
A	claim 1 column 3, line 45,46 -----	90

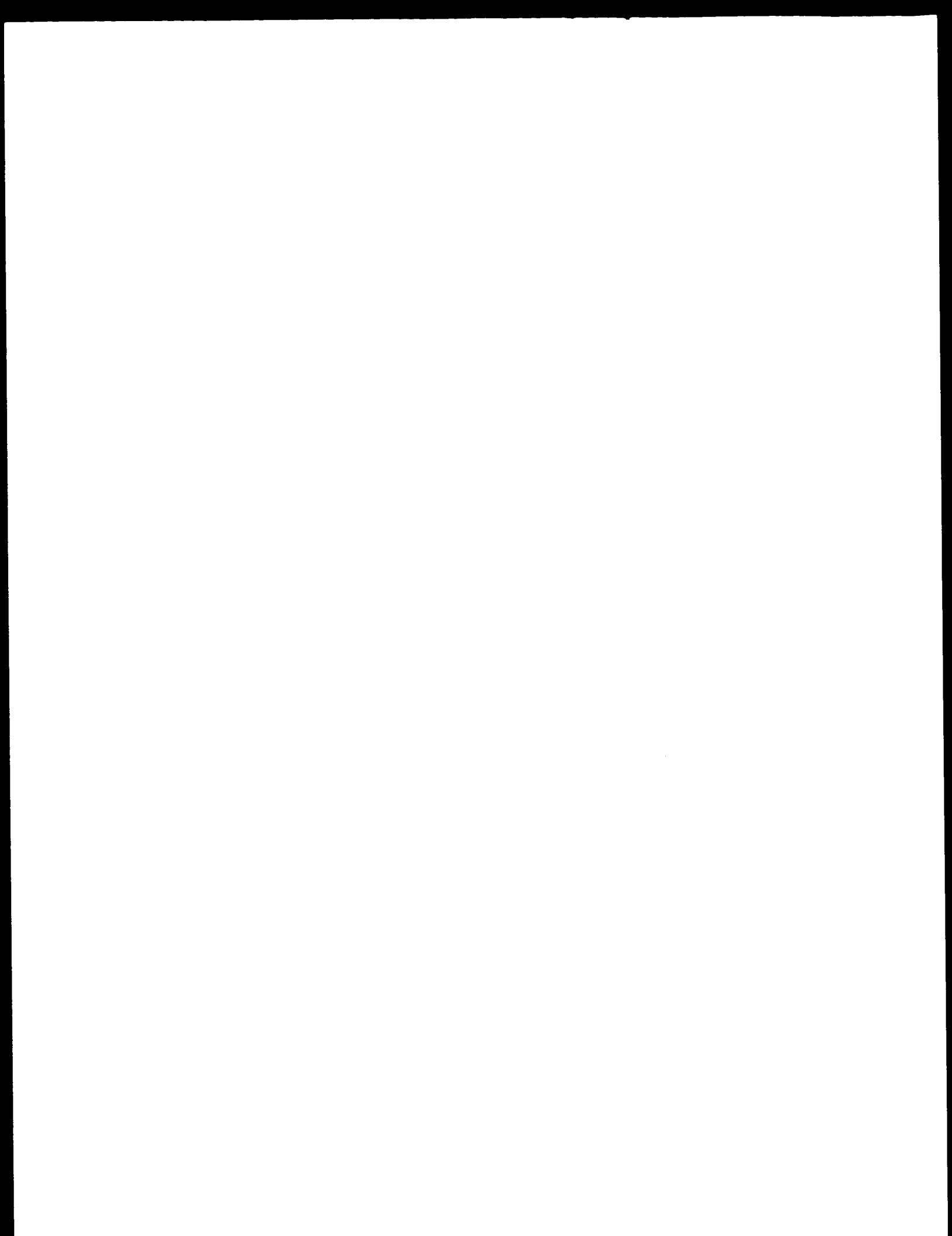


INTERNATIONAL SEARCH REPORT

Information on patent family members

 International Application No
 PCT/JP 00/00510

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
US 2458420	A	04-01-1949	NONE		
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JP 6247917	A	06-09-1994	NONE		
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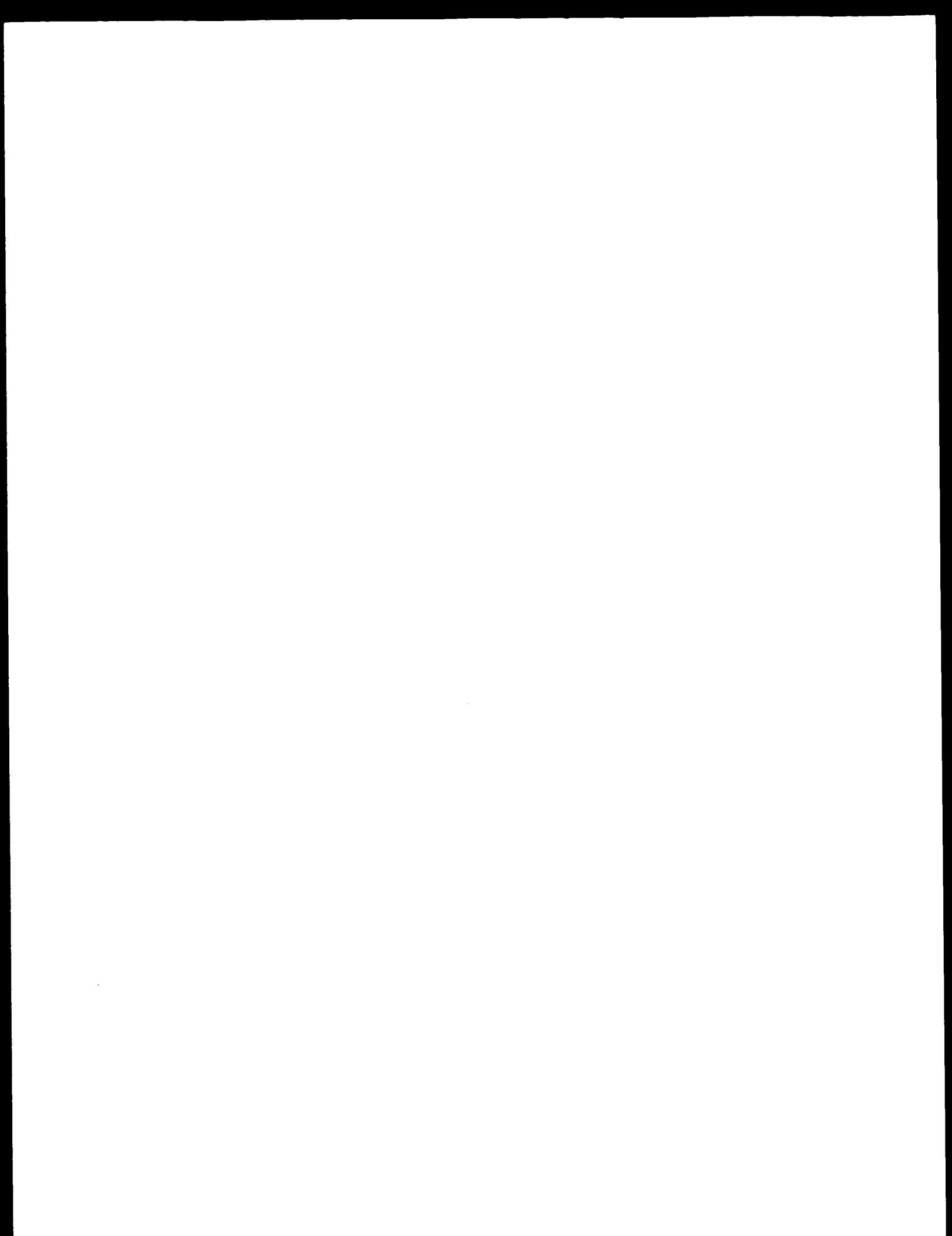
INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 00/00510

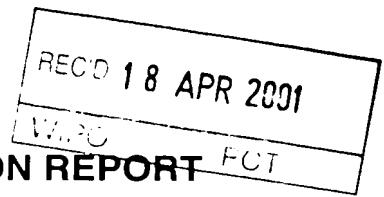
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PATENT COOPERATION TREATY

PCT**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

(PCT Article 36 and Rule 70)



5

Applicant's or agent's file reference YCT-469	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP00/00510	International filing date (<i>day/month/year</i>) 31/01/2000	Priority date (<i>day/month/year</i>) 29/01/1999	
International Patent Classification (IPC) or national classification and IPC C08F20/36			
<p>Applicant AMERSHAM PHARMACIA BIOTECH K.K. et al.</p> <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 9 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 54 sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input checked="" type="checkbox"/> Lack of unity of invention V <input type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input checked="" type="checkbox"/> Certain documents cited VII <input checked="" type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application 			

Date of submission of the demand 10/07/2000	Date of completion of this report 12.04.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Lux, R Telephone No. +49 89 2399 8593





INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP00/00510

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):
- Description, pages:**

1-7,10-12,14-28,	as originally filed		
30-37,39-55,			
57-98			
9,13,38,56	as received on	06/02/2001 with letter of	06/02/2001
8,29	as received on	13/02/2001 with letter of	09/02/2001

Claims, pages:

105-110,132,135,	as originally filed		
137,139-151,			
154-156			
103,119,125	as received on	06/02/2001 with letter of	06/02/2001
99,100,100a,101,	as received on	13/02/2001 with letter of	09/02/2001
101a,102,102a,104,			
111,111a,112,112a,			
113-118,118a,120,			
120a,121,122,122a,			
123,124,124a,126,			
127,127a,128,129,			
129a,130,130a,131,			
133,133a,134,136,			
136a,138,152,153,			
153a			

Drawings, sheets:

1/15-15/15	as originally filed
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2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
 the language of publication of the international application (under Rule 48.3(b)).



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- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
- 3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
 - contained in the international application in written form.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority in written form.
 - furnished subsequently to this Authority in computer readable form.
 - The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
- 4. The amendments have resulted in the cancellation of:
 - the description, pages:
 - the claims, Nos.:
 - the drawings, sheets:
- 5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c));
(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)
- 6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
 - the entire international application.
 - claims Nos. .

because:

- the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):



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see separate sheet

- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - no international search report has been established for the said claims Nos. .
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- the written form has not been furnished or does not comply with the standard.
 - the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:
 - restricted the claims.
 - paid additional fees.
 - paid additional fees under protest.
 - neither restricted nor paid additional fees.
2. This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
 - complied with.
 - not complied with for the following reasons:
see separate sheet
4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:
 - all parts.
 - the parts relating to claims Nos. see Item III..

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or



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2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet



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Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

A lack of clarity and conciseness of the claims as a whole arises, since the plurality of independent claims (35!) makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection. This objection is also of particular relevance having regard to the multiplicity of embodiments covered by claim 1 which includes **about 30** subgroups of different polymers (see Item IV.).

This deficiency could have been remedied by filing an amended set of claims defining the relevant subject-matter in terms of a minimum number of independent claims in each category followed by dependent claims covering features which are merely optional (Rule 6.4 PCT). However, the applicants choose not to do so.

Re Item IV

Lack of unity of invention

There is a lack of unity of the invention a posteriori.

The single inventive concept of this application may be represented by the fact that the polymers are "temperature-responsive" (whatever this obscure term may mean) due to certain functional groups being attached to the polymer backbone.

Most of the groups of polymers A through E-5 defined in independent claim 1 are already known from the "X" citations of the S.R.. In particular reference is made to:

D1 (US-A-2 458 420; see eg col. 1 and col. 3 line 11),

D3 (EP-A-0 697 400; see eg page 5 lines 40-55),

D6 (US-A-3 721 565; see eg col. 13 lines 6-8, and comonomers No. 136-139, 140 on col. 17, and claim 1),

D7 (US-A-4 062 831; see eg col. 2 lines 15-68, Examples 3 and 12), and

D13 (GB-A-1 409 967; see eg claim 1 wherein R² may acyl or carboxyalkyl)

which all disclose polymers having either ester and/or amido and/or ether groups attached to the polymer backbone.



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The requisite unity of invention (Rule 13.1 PCT) therefore no longer exists inasmuch as a technical relationship involving one or more of the same or corresponding special technical features in the sense of Rule 13.2 PCT does not exist between the groups of polymers specified in claim 1.

The separate inventions thus are:

- 1) Polymers A having an amido group attached to the polymer backbone via an ester group,
- 2) Polymers A having an ester group attached to the polymer backbone via an amido group,
- 3) Polymers A having attached to the polymer backbone diester groups,
- 4) Polymers B having attached to the polymer backbone diamido groups,
- 5) Polymers C-1 having attached to the polymer backbone amido group(s) and being crosslinked via one amido group,
- 6) Polymers C-1 having attached to the polymer backbone ester group(s) and being crosslinked via one ester group,
- 7) Polymers C-1 having attached to the polymer backbone ether group(s) and being crosslinked via one ether group,
- 8) Polymers C-1 having attached to the polymer backbone amido and ester groups and being crosslinked via one amido group,
- 9) Polymers C-1 having attached to the polymer backbone amido and ester groups and being crosslinked via one ester group,
- 10) Polymers C-1 having attached to the polymer backbone amido and ether groups and being crosslinked via one amido group,
- 11) Polymers C-1 having attached to the polymer backbone amido and ether groups and being crosslinked via one ether group,
- 12) Polymers C-1 having attached to the polymer backbone ester and ether groups and being crosslinked via one ester group,
- 13) Polymers C-1 having attached to the polymer backbone ester and ether groups and being crosslinked via one ether group,
- 14) Polymers C-1 having attached to the polymer backbone amido and ester and ether groups and being crosslinked via one amido group,
- 15) Polymers C-1 having attached to the polymer backbone amido and ester and ether groups and being crosslinked via one ester group,



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- 16) Polymers C-1 having attached to the polymer backbone amido and ester and ether groups and being crosslinked via one ether group,
- 17) Polymers C-2 having attached to the polymer backbone a diamido group,
- 18) Polymers C-2 having an amido group attached to the polymer backbone via an ester group,
- 19) Polymers C-2 having an amido group attached to the polymer backbone via an ether group,
- 20) Polymers D having attached to the polymer backbone an amido group,
- 21) Polymers E-1 having attached to the polymer backbone amido groups including a tertiary amido group,
- 22) Polymers E-2 having attached to the polymer backbone amido groups including a tertiary amido group,
- 23) Polymers E-2 having attached to the polymer backbone amido groups and ester groups including a tertiary amido group,
- 24) Polymers E-3 having attached to the polymer backbone amido groups including a tertiary amido group,
- 25) Polymers E-4 having attached to the polymer backbone amido groups including a tertiary amido group,
- 26) Polymers E-4 having attached to the polymer backbone amido groups and ester groups including a tertiary amido group,
- 27) Polymers E-5 having tertiary amido groups attached to the polymer backbone via amido groups,
- 28) Polymers E-5 having tertiary amido groups attached to the polymer backbone via ester groups, and
- 29) Polymers E-5 having tertiary amido groups attached to the polymer backbone via amido and ester groups.

The applicants did not comment upon this objection nor amended the claims in this respect.

Re Item VI

Certain documents cited

EP-A-0 970 945 and WO 00/07002: These documents may become relevant for novelty considerations when entering the regional phase.



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Re Item VII

Certain defects in the international application

It is noted that the applicants did not confirm that all disclaimers ("provisos") introduced into the amended set of claims have been drafted correctly and in close relation to the language and disclosure of the corresponding documents ie it was not confirmed that the disclaimers would not add new subject-matter as required by Art. 19 (2) PCT.

Further, there are the following deficiencies:

1. Line 28 of page 99 of original claim 1 is missing in new claim 1.
2. The reason for introducing into claims 1, 2, 9, 12, 13, and 16 the proviso "R is not derived from the structure of an amino acid" is not evident and has not been explained.
3. Part of line 18 of page 120 (see original claim 16) is missing in new claim 16.
4. The structures of group B has not been corrected in claim 30 (cf. page 128).
5. Part of line 26 of page 129 (se original claim 33) is missing in new claim 33.
6. The first line of original claim 48 is missing on new page 138.

